

#### FIELD OF THE INVENTION

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The present invention relates to a method and a detector for detecting human papilloma viruses, and more particularly to a method and a detector for simultaneously detecting and identifying subtype of human papilloma viruses.

#### BACKGROUND OF THE INVENTION

Cervical cancer is the most common cancer in women. The consorts are often men with penile warts. Sexual activity appears to be an important predisposing factor of the epidemic disease and precancerous lesions. In early 5 to 10 years during the development of cervical cancer, cervical cells form cervical intraepithelial neoplasm.

Recently, in order to decrease the incidence of cervical cancer, Pap smear is used for the cervical cancer screening. However, the Pap smear has a false negative rate of about 30%~40%. In addition, it is known that more that 95% of cervical carcinoma tissue contain detectable DNA sequences for known varieties of the human papilloma virus (HPV). Hence, the combination of Pap smear and HPV detection for the cervical cancer screening is considered.

The applicant cooperates with the hospital to did the epidemiolory research in women cervical cancer by using Pap smear and HPV detection, wherein the HPV detection is proceeded by using polymerase chain reaction and nucleotide sequencing. There are 2424 women aged from 16 to 84 for the epidemiology research, wherein 1963 women provide the effective specimen. The research results are shown as follows.

- 1) 1.9% (37/1963) of the women have abnormal cytological smears.
- 2) 12.7% (244/1926) of the women with normal cytological smears but have HPV infection.
- 25 3) The HPV prevalence in the women with abnormal cytological smears is 51.4% (19/37) and positively relative to the degree of the abnormal cytological smears, wherein the incidence of

abnormal non-typical squamous cells is 23.1%, the incidence of low abnormal epithelial cells is 41.7%, and the incidence of high abnormal epithelial cells is 75%.

4) The subtypes of human papilloma viruses detected in the specimens are HPV 52, HPV 58, HPV 70, HPV 16, HPV 18, HPV 68, HPV 33, HPV 66, HPV 35, HPV 37, HPV 54, HPV 59, HPV 67, HPV 72, HPV 69, HPV 82, HPV 39, HPV 31, HPV 32, HPV HLT7474-S, HPV 6, HPV CP8061, HPV 62, HPV CP8304, HPV 44, HPV 11, HPV 61, HPV 74, HPV 42 and HPV 43.

The conventional HPV detecting kits are only used for detecting 18 subtypes of human papilloma viruses including high risk HPV 16, HPV 18, HPV 31, HPV 33, HPV 35, HPV 39, HPV 45, HPV 51, HPV 52, HPV 56, HPV 58, HPV 59 and HPV 68, and detecting low risk HPV 6, HPV 11, HPV 42, HPV 43 and HPV 44.

According to the comparison of the epidemiology research and the conventional HPV detecting kits, various subtypes of human papilloma viruses contained in a specimen would not be identified by the conventional HPV detecting kits. In addition, the conventional HPV detecting kits are only used for detecting the high risk HPV and the low risk HPV, but not for identifying the HPV subtypes. Furthermore, the conventional HPV detecting kits lack the system control for checking the house-keep genes contained in a specimen.

In order to overcome the foresaid drawbacks of the conventional HPV detecting kits, the present invention provides a method and a detector for simultaneously detecting and identifying subtypes of human papilloma viruses contained in a sample.

## SUMMARY OF THE INVENTION

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It is therefore an object of the present invention to provide a detector for simultaneously detecting and identifying subtypes of human papilloma viruses (HPV) contained in a sample.

In accordance with the present invention, the detector includes a carrier having a first part and a second part for carrying the sample thereon, a first oligonucleotide carried on said first part of the carrier, and a second oligonucleotide carried on the second part of the carrier, wherein the first and second oligonucleotides respectively hybridized with deoxyribonucleic acids contained in a first subtype of human papilloma virus and a second subtype of human papilloma virus for simultaneously detecting and identifying subtypes of human papilloma viruses.

Preferably, the carrier is made of nylon.

Preferably, the carrier is a glass plate.

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Preferably, the first and second subtypes of human papilloma viruses are respectively selected from 38 subtypes of human papilloma viruses, wherein the sequence of the first oligonucleotide is selected from one of the sequence group corresponding to the first subtype of human papilloma virus and complementary sequences thereof, and the sequence of the second oligonucleotide is selected from one of the sequence group corresponding to the second subtype of human papilloma virus and complementary sequences thereof.

Preferably, the detector could be an oligonucleotide chip.

In another aspect of the present invention to provide a method for simultaneously detecting and identifying subtypes of human papilloma viruses contained in a sample.

In accordance with the present invention, the method includes steps of providing a first oligonucleotide and a second oligonucleotide for respectively hybridizing with a first and a second subtypes of human papilloma viruses, hybridizing deoxyribonucleic acid (DNA) contained in the sample with the first and second oligonucleotides, and removing nonhybridized DNA, thereby the subtypes of human papilloma viruses contained in the sample are detected and identified.

Preferably, the DNA contained in the sample is the product of polymerase chain reaction (PCR).

Preferably, the DNA contained in the sample has signaling substances labeled thereon.

Preferably, the signaling substance is biotin.

In addition, the method further includes a step of performing a reaction of biotin and avidinalkalinephosphatase.

On the other hand, the signaling substances could be fluorescent substances. Preferably, the fluorescent substance is Cyanine 5.

It is another aspect of the present invention to provide a method for detecting a subtype of human papilloma viruses contained in a sample.

In accordance with present invention, the method includes steps of providing an oligonucleotide complementary to a sequence specific to the subtype of human papilloma viruses, hybridizing said oligonucleotide with deoxyribonucleic acid (DNA) contained in the sample, removing non-hybridized DNA contained in the sample, and detecting hybridized DNA to show whether the subtype of human papilloma viruses contained in the sample.

The present invention may best be understood through the following descriptions with reference to the accompanying drawings, in which:

## BRIEF DESCRIPTION OF THE DRAWINGS

- Fig. 1 is a schematic view showing the detector according to the first preferred embodiment of the present invention;
- Fig. 2 is a schematic view showing the detector according to the second preferred embodiment of the present invention;
- Fig. 3(a) is a schematic view showing the detector according to the third preferred embodiment of the present invention;
  - Fig. 3(b) is a schematic view illustrating the subtype of human papilloma viruses identified by each dot shown in Fig. 3(a);
- Fig. 4(a) is the electrophoresis result showing the analyzed products of the first polymerase chain reaction;
  - Fig. 4(b) is the electrophoresis result showing the analyzed products of the second polymerase chain reaction;
  - Fig. 4(c) is detecting result on the detectors of detecting the HPV positive clones according to the third preferred embodiment of the present invention;
- Fig. 5 is a view showing the detecting result on the detectors of detecting samples according to the third preferred embodiment of the present invention;

Fig. 6(a) is a schematic view showing the detector according to the fourth preferred embodiment of the present invention;

Fig. 6(b) is a schematic view illustrating the subtype of human papilloma viruses identified by each dot shown in Fig. 6(a);

Fig. 7(a) is a view showing the detector stained with SYBR Green II according to the fourth embodiment of the present invention; and

Fig. 7(b) is a view showing the detecting result on the detectors of detecting samples according to the fourth preferred embodiment of the present invention.

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Please refer to Fig. 1. A detector 10 is the first embodiment of the present invention for simultaneously detecting and identifying the subtypes of human papilloma viruses contained in a sample. The detector 10 includes a carrier 11 and a dot array. The carrier 11 is a nylon membrane having the dot array 12 mounted thereon. Each dot in the dot array 12 is an oligonucleotide (15~30mer) for identifying a specific subtype of human papilloma viruses.

The sequences of the oligonucleotides provided by the present invention are specific to the epidemics of human papilloma viruses. The sequences of the oligonucleotides shown in Tables 1 to 38 are determined by the way of comparing DNA sequences of 97 subtypes of human papilloma viruses. Each table illustrates a plurality of oligonucleotides for identifying a specific subtype of human papilloma viruses.

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# METHOD AND DETECTOR FOR IDENTIFYING SUBTYPES OF HUMAN PAPILLOMA ${\tt VIRUSES}$

# 5 Table 1. Sequences and loci of oligonucleotides for identifying HPV 11

| SEQ ID NO:   | 5'→ 3'                        | Locus in HPV |
|--------------|-------------------------------|--------------|
|              |                               | 11           |
| SEQ ID NO:1  | ATCTGTGTCTAAATC               | .6799 –6813  |
| SEQ ID NO:2  | TCTGTGTCTAAATCTGCTAC          | 6800 - 6819  |
| SEQ ID NO:3  | ATCTGTGTCTAAATCTGCTACATACA    | 6799 – 6824  |
| SEQ ID NO:4  | TGCATCTGTGTCTAAATCTG          | 6796 – 6815  |
| SEQ ID NO:5  | AAATCTGCTACATACACTAA          | 6809 - 6828  |
| SEQ ID NO:6  | CTAAATCTGCTACATACACTA         | 6807 - 6827  |
| SEQ ID NO:7  | CTACATACACTAATTCAGAT          | 6816 6835    |
| SEQ ID NO:8  | TAGCATTACATTATCTGCAGAAG       | 6895 – 6917  |
| SEQ ID NO:9  | TCCTTCTGTTTTGGAGGAC           | 6943 – 6961  |
| SEQ ID NO:10 | TTTATCGCCTCCACCAAATGGTACAC    | 6973 – 6998  |
| SEQ ID NO:11 | TTATAGATATGTACAGTCACAGGCC     | 7009 – 7033  |
| SEQ ID NO:12 | ACCCACACCTGAAAAAGAAAAAC       | 7048 - 7070  |
| SEQ ID NO:13 | GGCGGATGCTCATTATGCGACTG       | 1044 - 1066  |
| SEQ ID NO:14 | ATATGTAAGTCCTATAAGCAATGTAG    | 1101 - 1126  |
| SEQ ID NO:15 | CTAATGCAGTAGAAAGTGAGATAAGT    | 1127 - 1152  |
| SEQ ID NO:16 | CACGGTTAGACGCCATTAAACTTACA    | 1154 - 1179  |
| SEQ ID NO:17 | CACAGCCAAAAAAGGTAAAGCGACGG    | 1181 - 1206  |
| SEQ ID NO:18 | GCAACGCAGGTAGAGAAACATGGCGA    | 1264 - 1289  |
| SEQ ID NO:19 | GAAAATGGGGAGATGGTCAGGAAAGGGAC | 1294 - 1323  |
| SEQ ID NO:20 | GACACAGGGAGGCACATAGAGGGTGA    | 1321 - 1346  |
| SEQ ID NO:21 | ACATAGAGAGGCGGAAGCAGTAGACG    | 1356 - 1381  |
| SEQ ID NO:22 | ACAGCACCGAGAGCATGCAGACACA     | 1382 - 1407  |
| SEQ ID NO:23 | TCAGGAATATTAGAATTACTAAAATG    | 1408 - 1433  |
| SEQ ID NO:24 | GCTGTCATTTGTTGATTTA           | 1482 - 1500  |

Table 2. Sequences and loci of oligonucleotides for identifying HPV 16

| SEQ ID NO:   | 5'→ 3'                 | Locus in HPV |
|--------------|------------------------|--------------|
|              |                        | 16           |
| SEQ ID NO:25 | TATGTCATTATGTGCTGCCA   | 6659 – 6678  |
| SEQ ID NO:26 | GTGCTGCCATATCTACTTCA   | 6670 – 6689  |
| SEQ ID NO:27 | TGCCATATCTACTTC        | 6674 – 6688  |
| SEQ ID NO:28 | TATCTACTTCAGAAACTACA   | 6679 – 6698  |
| SEQ ID NO:29 | CTACTTCAGAAACTACATATAA | 6682 – 6703  |

| SEQ ID NO:30 | ATAAAAATACTAACTTTAAG           | 6700 – 6719 |
|--------------|--------------------------------|-------------|
| SEQ ID NO:31 | CAAAATAACCTTAACTGCAGACG        | 6773 – 6795 |
| SEQ ID NO:32 | TTCCACTATTTTGGAGGAC            | 6821 – 6839 |
| SEQ ID NO:33 | TCTACAACCTCCCCAGGAGGCACAC      | 6851 – 6876 |
| SEQ ID NO:34 | TTATAGGTTTGTAACCCAG            | 6887 – 6905 |
| SEQ ID NO:35 | ACATACACCTCCAGCACCT            | 6923 – 6941 |
| SEQ ID NO:36 | CCTTAAAAAATACACT               | 6956 – 6971 |
| SEQ ID NO:37 | AGCAAAACAACATAGAGATGCAG        | 1089 - 1111 |
| SEQ ID NO:38 | ACTTAGTGATATTAGTGGATGTGTAG     | 1145 - 1170 |
| SEQ ID NO:39 | TAGTCCTAGATTAAAAGCTATATGTATAGA | 1181 - 1210 |
| SEQ ID NO:40 | GAAAAACAAAGTAGAGCTGCAAAAAG     | 1209 - 1234 |
| SEQ ID NO:41 | CTCAGCAGATGTTACAGGTAGAAGGG     | 1285 - 1310 |
| SEQ ID NO:42 | CCATGAGACTGAAACACCATGTAGTC     | 1313 - 1338 |
| SEQ ID NO:43 | GGGGGTGGTTGCAGTCAGTACAGTAG     | 1356 - 1381 |
| SEQ ID NO:44 | GTGGGGAGAGGGTGTTAGTGAAAGA      | 1387 - 1412 |
| SEQ ID NO:45 | CTATATGCCAAACACCACTTACAAAT     | 1417 - 1442 |
| SEQ ID NO:46 | GTTATACGGGGTGAGTTTTTCAGAAT     | 1502 - 1527 |
|              |                                |             |

Table 3. Sequences and loci of oligonucleotides for identifying HPV 18

| SEQ ID NO:   | 5'→ 3'                         | Locus in HPV |
|--------------|--------------------------------|--------------|
|              |                                | 18           |
| SEQ ID NO:47 | TTCTACACAGTCTCC                | 6650 – 6664  |
| SEQ ID NO:48 | CAGTCTCCTGTACCTGGGCA           | 6657 – 6676  |
| SEQ ID NO:49 | AGTCTCCTGTACCTGGGCAA           | 6658 – 6677  |
| SEQ ID NO:50 | TCTCCTGTACCTGGGCAATATGA        | 6660 – 6682  |
| SEQ ID NO:51 | CTGTACCTGGGCAATATGAT           | 6664 – 6683  |
| SEQ ID NO:52 | ATGATGCTACCAAATTTAAG           | 6679 – 6698  |
| SEQ ID NO:53 | TACTATTACTTTAACTGCAGATG        | 6752 - 6774  |
| SEQ ID NO:54 | TAGCAGTATTTTAGAGGAT            | 6800 – 6818  |
| SEQ ID NO:55 | TGTTCCCCCCCCCCAACTACTAGTT      | 6830 – 6855  |
| SEQ ID NO:56 | ATATCGTTTTGTACAATCTGTT         | 6866 – 6887  |
| SEQ ID NO:57 | GGATGCTGCACCGGCTGAA            | 6905 – 6923  |
| SEQ ID NO:58 | CTATGATAAGTTAAAG               | 6935 – 6950  |
| SEQ ID NO:59 | GGTCCACAATGATGCACAAGTGT        | 1135 - 1157  |
| SEQ ID NO:60 | CACAGAAAACAGTCCATTAGGGGAGC     | 1192 - 1217  |
| SEQ ID NO:61 | GCTGGAGGTGGATACAGAGTTAAGTC     | 1219 - 1244  |
| SEQ ID NO:62 | AGTGGGCAGAAAAAGGCAAAAAGGCGGCTG | 1271 - 1300  |
| SEQ ID NO:63 | CACAGATTCAGGTAACTACAAATGGC     | 1347 - 1372  |
| SEQ ID NO:64 | CAATGTATGTAGTGGCGGCAGTACGG     | 1384 - 1409  |
| SEQ ID NO:65 | GACAACGGGGCACAGAGGGCAACAA      | 1418 - 1443  |
| SEQ ID NO:66 | GTAGACGGTACAAGTGACAATAGCAA     | 1451 - 1476  |
| SEQ ID NO:67 | CCACAATGTACCATAGCACAATTAAA     | 1493 - 1518  |

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|------------------|----------------------------|---------------------|
| OTO TO MO CO     |                            | 1 4 5 5 5 4 5 6 6 1 |
| NELL III NILI'6X | CACATATGGGCTATCATTTACAGATT | 1573 - 1598         |
|                  | CACATATOGGCTATCATTTACAGATT | 1 10/0 - 10/0 1     |
|                  |                            |                     |

Table 4. Sequences and loci of oligonucleotides for identifying HPV 26

| SEQ ID NO:   | 5'→ 3'                         | Locus in    |
|--------------|--------------------------------|-------------|
|              |                                | HPV 26      |
| SEQ ID NO:69 | TAGTACATTATCTGCAGCAT           | 6619 – 6638 |
| SEQ ID NO:70 | ATTATCTGCAGCATC                | 6625 - 6639 |
| SEQ ID NO:71 | TGCAGCATCTGCATCCACTC           | 6631 - 6650 |
| SEQ ID NO:72 | GCATCTGCATCCACTCCATTTAAA       | 6635 – 6658 |
| SEQ ID NO:73 | CTCCATTTAAACCATCTGAT           | 6648 – 6667 |
| SEQ ID NO:74 | TAAAATAACACTTACAACAGATG        | 6727 – 6749 |
| SEQ ID NO:75 | TGCCTCCATATTGGAGGAT            | 6775 – 6793 |
| SEQ ID NO:76 | ACTAACCTTACCTCCCACTGCTAGTT     | 6805 - 6830 |
| SEQ ID NO:77 | CTATAGGTTTATTAAAAACTCT         | 6841 - 6862 |
| SEQ ID NO:78 | TAACGCCCCTCCTGTGCCA            | 6880 - 6898 |
| SEQ ID NO:79 | AAAACAGGCAAATACAAAGGCAG        | 1093 - 1115 |
| SEQ ID NO:80 | CTAGGTAGTCAGAACAGCCCGTTGCA     | 1139 - 1164 |
| SEQ ID NO:81 | GCGACAGTCAGCAGAATACACACCAAGTAA | 1194 - 1223 |
| SEQ ID NO:82 | CAAAAGGAGAGCCGTGGACAGTGTAC     | 1237 - 1262 |
| SEQ ID NO:83 | CCGTACAGGTAGATAAACAATATGAA     | 1305 - 1330 |
| SEQ ID NO:84 | GCCTAGTGTGTAGTCAGGGGGGG        | 1345 - 1369 |
| SEQ ID NO:85 | GCCTCAGTGGAAGATATCGATGTAGA     | 1376 - 1401 |
| SEQ ID NO:86 | CAGTGTTACACAAATATGTGAATTAT     | 1414 - 1439 |
| SEQ ID NO:87 | CAGTATATGGTGTAAGTTTTGCAGAA     | 1485 - 1510 |

Table 5. Sequences and loci of oligonucleotides for identifying HPV 31

| SEQ ID NO:    | 5'→ 3'                         | Locus in HPV 31 |
|---------------|--------------------------------|-----------------|
| SEQ ID NO:88  | TGCAATTGCAAACAG                | 6592 - 6606     |
|               |                                |                 |
| SEQ ID NO:89  | GCAATTGCAAACAGTGATAC           | 6593 – 6612     |
| SEQ ID NO:90  | CAATTGCAAACAGTGATACT           | 6594 – 6613     |
| SEQ ID NO:91  | GCAAACAGTGATACTACATTTAA        | 6599 – 6621     |
| SEQ ID NO:92  | CTACATTTAAAAGTAGTAAT           | 6612 – 6631     |
| SEQ ID NO:93  | CAAAATAACATTATCTGCAGACA        | 6691 – 6713     |
| SEQ ID NO:94  | TCCTGCTATTTTGGAAGAT            | 6739 – 6757     |
| SEQ ID NO:95  | ATTGACCACACCTCCCTCAGGTTCTT     | 6769 – 6794     |
| SEQ ID NO:96  | CTATAGGTTTGTCACCTCACAG         | 6805 - 6826     |
| SEQ ID NO:97  | AACTGCCCCCAAAAGCCC             | 6844 – 6862     |
| SEQ ID NO:98  | AGCGGAGGAACATGCAGAGGCTG        | 1083 - 1105     |
| SEQ ID NO:99  | TTTAAGTGATATTAGTAGTTGTGTGG     | 1140 - 1165     |
| SEQ ID NO:100 | AGTCCACGGTTAAAAGCTATATGCATAGAA | 1177 - 1206     |
| SEQ ID NO:101 | GACTCTTTGAACTTCCAGACAGCGGG     | 1232 - 1257     |

| SEQ ID NO:102 | GCAGCAGATGGTACAGGTAGAGGAGC | 1281 - 1306 |
|---------------|----------------------------|-------------|
| SEQ ID NO:103 | AATGGTAGTGACGGGACACATAGTGA | 1327 - 1352 |
| SEQ ID NO:104 | CCAACACGTAATATATTGCAAGTGTT | 1369 - 1394 |
| SEQ ID NO:105 | GCAATGGTAAAGCTGCTATGTTAGGT | 1403 - 1428 |
| SEQ ID NO:106 | TTATATGGTGTAAGTTTTATGGAAC  | 1441 - 1465 |

Table 6. Sequences and loci of oligonucleotides for identifying HPV 32

| SEQ ID NO:    | 5'→ 3'                         | Locus in<br>HPV 32 |
|---------------|--------------------------------|--------------------|
| SEQ ID NO:107 | TGCTACTGTAACAACTGAAG           | 6906 – 6925        |
| SEQ ID NO:108 | GCTACTGTAACAACTGAAGA           | 6907 – 6926        |
| SEQ ID NO:109 | TACTGTAACAACTGA                | 6909 – 6923        |
| SEQ ID NO:110 | ACTGTAACAACTGAAGACAC           | 6910 – 6929        |
| SEQ ID NO:111 | CAACTGAAGACACATACAAGTC         | 6917 – 6938        |
| SEQ ID NO:112 | CAAAATTACATTATCTGTAGAGG        | 7005 – 7027        |
| SEQ ID NO:113 | TCCTGACATACTAGACGAT            | 7053 – 7071        |
| SEQ ID NO:114 | TGTAGCTCCACCGCCCTCTGGTACTT     | 7083 – 7108        |
| SEQ ID NO:115 | TTATAGATTTGTGCAGTCTCAG         | 7119 –7140         |
| SEQ ID NO:116 | TAAGGTAACAGCACCTGAA            | 7158 – 7176        |
| SEQ ID NO:117 | TTTTTCTGACTATTCA               | 7188 – 7203        |
| SEQ ID NO:118 | AGCACATGCAGATAAGGAGGCAG        | 1062 - 1084        |
| SEQ ID NO:119 | GGCAGTCCATATGAAAGTCCCGCCAGTGAT | 1111 - 1140        |
| SEQ ID NO:120 | GAGCTAAGCCCTAGGCTTGGTGGATT     | 1162 - 1187        |
| SEQ ID NO:121 | GGGGCCAAACGACGACTATTTCAATC     | 1210 - 1235        |
| SEQ ID NO:122 | GCAGGAACAGGTAGAAAATGGACATG     | 1284 - 1309        |
| SEQ ID NO:123 | GTGTACATGGGGTGCAGGAAAATCAG     | 1352 - 1377        |
| SEQ ID NO:124 | GCCTACAACAAGGGTGGTGGAATTGC     | 1395 - 1420        |
| SEQ ID NO:125 | GCAAGCAACATTGTTAGGTAAGTTTA     | 1437 - 1462        |
| SEQ ID NO:126 | GCTGTTTGGATTGTCATTTGGTGATT     | 1467 - 1492        |

Table 7. Sequences and loci of oligonucleotides for identifying HPV 33

| SEQ ID NO:    | 5'→ 3'                     | Locus in HPV 33 |
|---------------|----------------------------|-----------------|
| SEQ ID NO:127 | TATGCACACAAGTAACTAGT       | 6624 - 6643     |
| SEQ ID NO:128 | CACACAAGTAACTAG            | 6628 - 6642     |
| SEQ ID NO:129 | ACAAGTAACTAGTGACAGTA       | 6631 - 6650     |
| SEQ ID NO:130 | GTAACTAGTGACAGTACATATAA    | 6635 – 6657     |
| SEQ ID NO:131 | GTACATATAAAAATGAAAAT       | 6648 – 6667     |
| SEQ ID NO:132 | CAAAGTTACCTTAACTGCAGAAG    | 6727 – 6749     |
| SEQ ID NO:133 | TCCAGATATTTTAGAAGAT        | 6775 – 6793     |
| SEQ ID NO:134 | TTTAACACCTCCTCCATCTGCTAGTT | 6805 - 6830     |
| SEQ ID NO:135 | CTATAGGTTTGTTACCTCTCAG     | 6841 - 6862     |

| SEQ ID NO:136 | AACAGTACCTCCAAAGGAA             | 6880 – 6898 |
|---------------|---------------------------------|-------------|
| SEQ ID NO:137 | CTTAGGTAAATATACA                | 6910 – 6925 |
| SEQ ID NO:138 | AGGGGAGGATGATTTAAATGCTG         | 1100 - 1122 |
| SEQ ID NO:139 | GCATGTTCACAAAGTGCTGCGGAGGA      | 1149 - 1174 |
| SEQ ID NO:140 | GATCGTGCTGCAAACCCGTGTAGAAC      | 1182 - 1207 |
| SEQ ID NO:141 | GAATGCACATACAGAAAAACGAAAAATAGAT | 1227 - 1256 |
| SEQ ID NO:142 | AAATAGATGAGCTAGAAGACAGCGGA      | 1249 - 1274 |
| SEQ ID NO:143 | GGTACAACAGGTAGAAAGTCAAAATG      | 1307 - 1332 |
| SEQ ID NO:144 | GACTTAGAATCTAGTGGGGTGGGGA       | 1350 - 1357 |
| SEQ ID NO:145 | CTGTGAGACAAATGTAGATAGCTGTG      | 1391 - 1416 |
| SEQ ID NO:146 | CGTTGCAGGAAATTAGTAATGTTCTA      | 1426 - 1451 |
| SEQ ID NO:147 | GAGGCCTATGGAATAAGTTTTAT         | 1494 - 1516 |

Table 8. Sequences and loci of oligonucleotides for identifying HPV 35

| SEQ ID NO:    | 5'→ 3'                         | Locus in HPV<br>35 |
|---------------|--------------------------------|--------------------|
| SEQ ID NO:148 | TCTGCTGTCTTCTAGTGA             | 6612 – 6631        |
| SEQ ID NO:149 | TGCTGTGTCTTCTAG                | 6614 – 6628        |
| SEQ ID NO:150 | GTGTCTTCTAGTGACAGTAC           | 6618 – 6637        |
| SEQ ID NO:151 | CTTCTAGTGACAGTACATATAAA        | 6622 – 6644        |
| SEQ ID NO:152 | GTACATATAAAAATGACAAT           | 6634 – 6653        |
| SEQ ID NO:153 | TAAAATAACACTAACAGCAGATG        | 6713 – 6735        |
| SEQ ID NO:154 | CCCGTCCATTTTAGAGGAT            | 6761 – 6779        |
| SEQ ID NO:155 | CCTTACACCACCGCCTTCTGGTACCT     | 6791 – 6816        |
| SEQ ID NO:156 | ATATCGCTATGTAACATCACAG         | 6827 – 6848        |
| SEQ ID NO:157 | ACCCAGTGCACCAAAACCT            | 6866 – 6884        |
| SEQ ID NO:158 | GGAGCAAACACACAAAGAGGCTG        | 1089 - 1111        |
| SEQ ID NO:159 | GCAGCGTGAGCTTATGTGTTAATAATAACA | 1151 - 1180        |
| SEQ ID NO:160 | GTCCACGTTTAAAAGCTATTTGCA       | 1184 - 1207        |
| SEQ ID NO:161 | CGATTATTTGAACTACCAGACAGCGG     | 1237 - 1262        |
| SEQ ID NO:162 | GAGATACAACAGGTAGAGGGGCATGA     | 1291 - 1316        |
| SEQ ID NO:163 | GGGCAGTGGGGATAGTATAACCTCTA     | 1338 - 1363        |
| SEQ ID NO:164 | GACATGATGAGACTCCAACGCGAGAC     | 1376 - 1401        |
| SEQ ID NO:165 | CTAAAATGTAGTAATGCAAACGCAGC     | 1414 - 1439        |
| SEQ ID NO:166 | GCTATGTTGGCTAAATTTAAAGAACT     | 1438 - 1463        |

Table 9. Sequences and loci of oligonucleotides for identifying HPV 37

| SEQ ID NO:    | 5'→ 3'               | Locus in HPV |
|---------------|----------------------|--------------|
|               |                      | 37           |
| SEQ ID NO:167 | TGTCTACTGACAATG      | 6782 – 6796  |
| SEQ ID NO:168 | TGTCTACTGACAATGGCGAA | 6782 - 6801  |
| SEQ ID NO:169 | TGACAATGGCGAAGTTACAG | 6789 – 6808  |

| SEQ ID NO:170 | GACAATGGCGAAGTTACAGA       | 6790 – 6809 |
|---------------|----------------------------|-------------|
| SEQ ID NO:171 | AATGGCGAAGTTACAGAATA       | 6793 - 6812 |
| SEQ ID NO:172 | CAGAATATAATTCTCAAACA       | 6806 – 6825 |
| SEQ ID NO:173 | TAAAGTTCCTTTAAAGGCTGAGG    | 6885 – 6907 |
| SEQ ID NO:174 | TTCTGGTATATTGGAAGAG        | 6933 – 6951 |
| SEQ ID NO:175 | ATTTGTACCTACTCCAGATAATTCAG | 6963 - 6988 |
| SEQ ID NO:176 | TTATAGGTACATTAATTCAAAG     | 6999 – 7020 |
| SEQ ID NO:177 | TGCAGTTGTTGAAAAAGAA        | 7038 – 7056 |
| SEQ ID NO:178 | CTTTGCAAAATATACA           | 7068 - 7083 |

Table 10. Sequences and loci of oligonucleotides for identifying HPV 39

| SEQ ID NO:    | 5'→ 3'                         | Locus in    |
|---------------|--------------------------------|-------------|
|               |                                | HPV 39      |
| SEQ ID NO:179 | CTCTATAGAGTCTTC                | 6677 – 6691 |
| SEQ ID NO:180 | TAGAGTCTTCCATACCTTCT           | 6682 – 6701 |
| SEQ ID NO:181 | ATAGAGTCTTCCATACCTTC           | 6681 – 6700 |
| SEQ ID NO:182 | GTCTTCCATACCTTCTACATATG        | 6686 – 6708 |
| SEQ ID NO:183 | CTACATATGATCCTTCTAAG           | 6700 – 6719 |
| SEQ ID NO:184 | TACTGTCACATTAACAACTGATG        | 6779 – 6801 |
| SEQ ID NO:185 | TTCCTCTATATTGGACAA             | 6827 - 6844 |
| SEQ ID NO:186 | TGTAGCTCCTCCACCATCTGCCAGTT     | 6857 – 6882 |
| SEQ ID NO:187 | TTACAGATACCTACAGTCTGCA         | 6893 – 6914 |
| SEQ ID NO:188 | GGATGCTCCAGCACCTGAA            | 6932 – 6950 |
| SEQ ID NO:189 | ATATGACGGTCTAAAG               | 6962 – 6977 |
| SEQ ID NO:190 | GGCCCAAAGGGATGCACAAGCAG        | 1149 - 1171 |
| SEQ ID NO:191 | CAGACAGCAGTGGCGACACTAGACCGTATG | 1196 – 1225 |
| SEQ ID NO:192 | GTAGGCAGGAATACCAGGGGAACAC      | 1234 - 1258 |
| SEQ ID NO:193 | GCAGTACGCAGGCAACACAAACGGTG     | 1283 - 1308 |
| SEQ ID NO:194 | GGAGGAGGTAACTGTAGCAACTAATA     | 1362 - 1387 |
| SEQ ID NO:195 | CATGGCGGCAGTGTACGGGAGGAGTG     | 1411 – 1436 |
| SEQ ID NO:196 | GGATAGTGCTATAGATAGTGAAAACC     | 1446 – 1471 |
| SEQ ID NO:197 | CTCCAACTGCACAAATTAAATTATTG     | 1484 – 1509 |
| SEQ ID NO:198 | CCAATAACAAAAAGGCTGCAATGCTA     | 1517 – 1542 |

Table 11. Sequences and loci of oligonucleotides for identifying HPV 44

| SEQ ID NO:    | 5'→ 3'                 | Locus in    |
|---------------|------------------------|-------------|
|               |                        | HPV 40      |
| SEQ ID NO:199 | TGCCACTACACAGTC        | 6719 – 6733 |
| SEQ ID NO:200 | CTACACAGTCCCCTCCGTCT   | 6724 – 6743 |
| SEQ ID NO:201 | TGCCACTACACAGTCCCCTC   | 6719 – 6738 |
| SEQ ID NO:202 | CAGTCCCCTCCGTCTACATATA | 6729 - 6750 |
| SEQ ID NO:203 | CTACATATACTAGTGAACAA   | 6742 - 6761 |

| SEQ ID NO:204 | TAGTATTACCTTAACGGCGGAGG        | 6821 - 6843 |
|---------------|--------------------------------|-------------|
| SEQ ID NO:205 | TGCTGGTATTTTAGAACAG            | 6869 – 6887 |
| SEQ ID NO:206 | GTTGTCGCCGCCCCAAATGGTACCT      | 6899 - 6924 |
| SEQ ID NO:207 | ATACAGATATGTGCAGTCCCAG         | 6935 – 6956 |
| SEQ ID NO:208 | GCCACCCCTGAAAAGGCA             | 6974 – 6992 |
| SEQ ID NO:209 | CTATGCAAAATTAAGT               | 7004 – 7019 |
| SEQ ID NO:210 | GGCGGATGCTCATTATGCGGCTG        | 1038 – 1060 |
| SEQ ID NO:211 | GGTAGTCCATATGTTAGTCCTTTAAGTAAT | 1087 – 1116 |
| SEQ ID NO:212 | CACGGCTGGACGCTATAACATTAAGT     | 1148 – 1173 |
| SEQ ID NO:213 | GACGGCTGTTTGACAGACCAGAATTA     | 1196 – 1221 |
| SEQ ID NO:214 | GCTGAAACGCAGGTAGAGAGAAATGG     | 1255 - 1280 |
| SEQ ID NO:215 | GGGAGGTGGACAAGGAAGGGACACAG     | 1299 1324   |
| SEQ ID NO:216 | GGAAGTGCAGACACATAGCAACACAC     | 1347 - 1372 |
| SEQ ID NO:217 | GGTACTAGAACTATTGAAATGTAAGA     | 1395 – 1420 |
| SEQ ID NO:218 | GCTTGGTAAGTTTAAGGATTGCTATG     | 1437 – 1462 |
|               |                                |             |

Table 12. Sequences and loci of oligonucleotides for identifying HPV 45

| SEQ ID NO:    | 5'→ 3'                         | Locus in    |
|---------------|--------------------------------|-------------|
|               |                                | HPV 45      |
| SEQ ID NO:219 | TGCCTCTACACAAAATCCTG           | 6651 – 6670 |
| SEQ ID NO:220 | CTCTACACAAAATCC                | 6654 – 6668 |
| SEQ ID NO:221 | ACAAAATCCTGTGCCAAGTA           | 6660 – 6679 |
| SEQ ID NO:222 | CAAAATCCTGTGCCAAGTAC           | 6661 – 6680 |
| SEQ ID NO:223 | AATCCTGTGCCAAGTACATATG         | 6664 – 6685 |
| SEQ ID NO:224 | GTACATATGACCCTACTAAG           | 6677 – 6696 |
| SEQ ID NO:225 | CACTATTACTTTAACTGCAGAGG        | 6756 – 6778 |
| SEQ ID NO:226 | TAGTAGTATATTAGAAAAT            | 6804 - 6822 |
| SEQ ID NO:227 | TGTCCCTCCACCACCTACTACAAGTT     | 6834 – 6859 |
| SEQ ID NO:228 | ATATCGTTTTGTGCAATCAGTT         | 6870 - 6891 |
| SEQ ID NO:229 | GGATACTACACCTCCAGAA            | 6909 – 6927 |
| SEQ ID NO:230 | AGTTCAGAATGATGCACAGGTGT        | 1135 - 1157 |
| SEQ ID NO:231 | GCAGCTAAGTGTGGATACGGATCTAAGTCC | 1216 – 1245 |
| SEQ ID NO:232 | CAAGAAATTTCATTAAATAGTGGGCA     | 1253 - 1278 |
| SEQ ID NO:233 | ACGGTTGTTTACAATATCAGATAGTG     | 1294 – 1319 |
| SEQ ID NO:234 | CATAGTACACAAAGTAGTGGTGGGGA     | 1397 – 1422 |
| SEQ ID NO:235 | GACAATGCAGAAAATGTAGATCCGCA     | 1430 – 1455 |
| SEQ ID NO:236 | GGAGCTATTACAAGCAAGTAACAAAA     | 1477 – 1502 |
| SEQ ID NO:237 | GCAATGCTGGCAGTATTTAAAGACA      | 1508 - 1532 |
| SEQ ID NO:238 | ATATGGGCTGTCATTTACGGATTTGG     | 1534 – 1559 |

Table 13. Sequences and loci of oligonucleotides for identifying HPV 51

| г |            |        |              |
|---|------------|--------|--------------|
| Ì | SEQ ID NO: | 5'→ 3' | Locus in HPV |

|               |                                | 51          |
|---------------|--------------------------------|-------------|
| SEQ ID NO:239 | CACTGCCACTGCTGCGGTTT           | 6555 – 6574 |
| SEQ ID NO:240 | TGCCACTGCTGCGGT                | 6558 - 6572 |
| SEQ ID NO:241 | CACTGCTGCGGTTTCCCCAA           | 6561 – 6580 |
| SEQ ID NO:242 | CCACTGCTGCGGTTTCCCCA           | 6560 – 6579 |
| SEQ ID NO:243 | CTGCGGTTTCCCCAACATTTAC         | 6566 – 6587 |
| SEQ ID NO:244 | CAACATTTACTCCAAGTAAC           | 6578 – 6597 |
| SEQ ID NO:245 | TAAAATTACTTTAACTACAGAGG        | 6657 – 6679 |
| SEQ ID NO:246 | TCCTACCATTCTTGAACAG            | 6705 – 6723 |
| SEQ ID NO:247 | ATTAACATTACCTCCGTCTGCTAGTT     | 6735 – 6760 |
| SEQ ID NO:248 | ATATAGGTTTGTTAGAAATGCA         | 6771 – 6792 |
| SEQ ID NO:249 | GGACACCCCTCCACAGGCT            | 6810 – 6828 |
| SEQ ID NO:250 | TTTGGCCAAATATAAA               | 6840 – 6855 |
| SEQ ID NO:251 | ATTACAGGCAAACAAAGAGGCTG        | 1092 – 1114 |
| SEQ ID NO:252 | GCGAAGCAGCCCATTAGGAGACATTACAAA | 1149 – 1178 |
| SEQ ID NO:253 | CCATAGTCAGGCAAACGAGTCACAAG     | 1197 – 1222 |
| SEQ ID NO:254 | AGATTACTGGACAGTTATCCGGACA      | 1231 – 1255 |
| SEQ ID NO:255 | CAGGTAGATGGCAACATGGCGGTTC      | 1300 – 1325 |
| SEQ ID NO:256 | AGCTGTGCAAATGTAGAACTAAACAG     | 1384 – 1409 |
| SEQ ID NO:257 | GGTATTAGTTATAATGAGTTGGTACG     | 1477 – 1502 |

Table 14. Sequences and loci of oligonucleotides for identifying HPV 52

| SEQ ID NO:    | 5'→ 3'                         | Locus in    |
|---------------|--------------------------------|-------------|
|               |                                | HPV 52      |
| SEQ ID NO:258 | TGAGGTTAAAAAGGA                | 6695 – 6709 |
| SEQ ID NO:259 | TGAGGTTAAAAAGGAAAGCA           | 6695 – 6714 |
| SEQ ID NO:260 | GAGGTTAAAAAGGAAAGCAC           | 6696 – 6715 |
| SEQ ID NO:261 | TTAAAAAGGAAAGCACATAT           | 6700 – 6719 |
| SEQ ID NO:262 | AAAGGAAAGCACATATAAAAAT         | 6704 6725   |
| SEQ ID NO:263 | GCACATATAAAAATGAAAAT           | 6712 – 6731 |
| SEQ ID NO:264 | CAAAATTACATTAACAGCTGATG        | 6791 – 6813 |
| SEQ ID NO:265 | TGCCACTATTTTAGAGGAC            | 6839 – 6857 |
| SEQ ID NO:266 | CCTTACCCCACCACCGTCTGCATCTT     | 6869 – 6894 |
| SEQ ID NO:267 | ATACAGATTTGTCACTTCTACT         | 6905 – 6926 |
| SEQ ID NO:268 | AAACACACCACCTAAAGGA            | 6944 – 6962 |
| SEQ ID NO:269 | TTTAAAGGACTATATG               | 6974 – 6989 |
| SEQ ID NO:270 | AGGGGAGGATGATTTACATGCTG        | 1085 - 1107 |
| SEQ ID NO:271 | GCAGTCCGGAAAGTGCTGGGCAAGATGGTG | 1135 - 1164 |
| SEQ ID NO:272 | GGTAGTCCGCGTGCAAAACACATTTG     | 1176 – 1201 |
| SEQ ID NO:273 | CCAAAACGCAAACCATGTCACGTAGA     | 1224 - 1249 |
| SEQ ID NO:274 | CAAAATGGCGACTGGCAAAGTA         | 1311 - 1332 |
| SEQ ID NO:275 | GCTAGTAATTCAGATGTAAGTTGTAC     | 1359 - 1384 |
| SEQ ID NO:276 | GAGGAAAATAGTAATAGAACGCTAAA     | 1401 – 1426 |

| SEQ ID NO:277 | GCGAAAATAGCATAAAAACAACTGTA | 1447 - 1472 |
|---------------|----------------------------|-------------|
| SEQ ID NO:278 | AGAAACATATGGTGTTAGCTTTATGG | 1487 - 1512 |

Table 15. Sequences and loci of oligonucleotides for identifying HPV 53

| SEQ ID NO:    | 5'→ 3'                     | Locus in HPV |
|---------------|----------------------------|--------------|
|               |                            | 53           |
| SEQ ID NO:279 | TCCGCAACCACAGTCTAT         | 6681 – 6700  |
| SEQ ID NO:280 | CCGCAACCACAGT              | 6682 – 6696  |
| SEQ ID NO:281 | CCGCAACCACACAGTCTATG       | 6682 – 6701  |
| SEQ ID NO:282 | CACAGTCTATGTCTACATATAA     | 6691 – 6712  |
| SEQ ID NO:283 | CTACATATAATTCAAAGCAA       | 6703 - 6722  |
| SEQ ID NO:284 | TAAAATATCCCTGTCTGCTGAGG    | 6782 – 6804  |
| SEQ ID NO:285 | TTCTACCTTACTGGAAGAC        | 6830 - 6848  |
| SEQ ID NO:286 | TTTGTCGCCTCCTGTTGCCACTAGCT | 6860 – 6885  |
| SEQ ID NO:287 | ATACAGATATGTGAAAAGTGCA     | 6896 – 6917  |
| SEQ ID NO:288 | GGATCAGCCCCCTCCTGAA        | 6935 - 6953  |

Table 16. Sequences and loci of oligonucleotides for identifying HPV 54

| SEQ ID NO:    | 5'→ 3'                         | Locus in<br>HPV 54 |
|---------------|--------------------------------|--------------------|
| SEQ ID NO:289 | TACAGCATCCACGCA                | 6633 – 6647        |
| SEQ ID NO:290 | CAGCATCCACGCAGGATAGC           | 6635 – 6654        |
| SEQ ID NO:291 | ACGCAGGATAGCTTTAATAA           | 6643 - 6662        |
| SEQ ID NO:292 | CACGCAGGATAGCTTTAATA           | 6642 – 6661        |
| SEQ ID NO:293 | ATAGCTTTAATAATTCTGAC           | 6650 – 6669        |
| SEQ ID NO:294 | TACCATAACCCTTACAGCAGATG        | 6729 – 6751        |
| SEQ ID NO:295 | TCCCACTATTCTAGAGGAC            | 6777 – 6795        |
| SEQ ID NO:296 | TATAACCCCCCAGCTACAAGTAGTT      | 6807 - 6832        |
| SEQ ID NO:297 | ATATAGGTTTGTACAGTCACAG         | 6843 – 6864        |
| SEQ ID NO:298 | GAATAATGCCCCTGCAAAGGAA         | 6882 – 6903        |
| SEQ ID NO:299 | GCTGCAGGCAGATGTAGAGGCAG        | 1043 - 1065        |
| SEQ ID NO:300 | CGTATGTAAGTCCTGTTGCAAACAGCGAAC | 1099 – 1128        |
| SEQ ID NO:301 | CTGTGTAGAAAAGGACCTAA           | 1130 - 1149        |
| SEQ ID NO:302 | TATATCCCTAGGACGGCGGTCAGCCA     | 1166- 1191         |
| SEQ ID NO:303 | GGTAAATACCGAGGGGACAGATGAAA     | 1265 – 1290        |
| SEQ ID NO:304 | GAAACAACTACAGATAGCCTAGGAAG     | 1323 - 1348        |
| SEQ ID NO:305 | CGTGTAGCATTGTTTGGTATGTTTAA     | 1386 – 1411        |
| SEQ ID NO:306 | TATGGATTAAGTTTTATGGACC         | 1419 – 1440        |

Table 17. Sequences and loci of oligonucleotides for identifying HPV 56

| SEQ ID NO: | 5'→3' | Locus in HPV |
|------------|-------|--------------|
|            | L     | <u> </u>     |

|                      |                            | 56          |
|----------------------|----------------------------|-------------|
| <b>SEQ ID NO:307</b> | CTGCTACAGAACAGT            | 6630 – 6644 |
| SEQ ID NO:308        | GCTACAGAACAGTTAAGTAA       | 6632 – 6651 |
| SEQ ID NO:309        | CAGAACAGTTAAGTAAATAT       | 6636 – 6655 |
| SEQ ID NO:310        | GAACAGTTAAGTAAATATGATGC    | 6638 – 6660 |
| SEQ ID NO:311        | GTAAATATGATGCACGAAAA       | 6648 – 6667 |
| SEQ ID NO:312        | CAAAATTACTTTGTCTGCAGAGG    | 6727 – 6749 |
| <u>SEQ ID NO:313</u> | TGCTAACCTACTGGAGGAC        | 6775 – 6793 |
| SEQ ID NO:314        | GTTATCCCCGCCAGTGGCCACCAGCC | 6805 - 5830 |
| SEQ ID NO:315        | ATATAGATATGTTAGAAGCACA     | 6841 – 6862 |
| SEQ ID NO:316        | GGAACAGCCACCAACAGAA        | 6880 – 6898 |

Table 18. Sequences and loci of oligonucleotides for identifying HPV 58

| SEQ ID NO:    | 5'→ 3'                         | Locus in HPV<br>58 |
|---------------|--------------------------------|--------------------|
| SEQ ID NO:317 | ATGCACTGAAGTAACTAAGG           | 6674 – 6693        |
| SEQ ID NO:318 | CACTGAAGTAACTAAGGAAG           | 6677 – 6696        |
| SEQ ID NO:319 | TGAAGTAACTAAGGA                | 6680 - 6694        |
| SEQ ID NO:320 | GAAGTAACTAAGGAAGGTAC           | 6681 – 6700        |
| SEQ ID NO:321 | CTAAGGAAGGTACATATAAAAA         | 6688 – 6709        |
| SEQ ID NO:322 | ATAAAAATGATAATTTTAAG           | 6703 - 6722        |
| SEQ ID NO:323 | CAAAATTACACTAACTGCAGAGA        | 6776 – 6798        |
| SEQ ID NO:324 | TTCCAATATTTTGGAGGAC            | 6824 – 6842        |
| SEQ ID NO:325 | TTTAACACCTCCTCCGTCTGCCAGTT     | 6854 - 6879        |
| SEQ ID NO:326 | ATATAGATTTGTTACCTCCCAG         | 6890 – 6911        |
| SEQ ID NO:327 | AACAGCACCCCTAAAGAA             | 6929 – 6947        |
| SEQ ID NO:328 | AGGGGTGGACGATATAAATGCTG        | 1104 – 1126        |
| SEQ ID NO:329 | GCATGCTCAGAAAGTGCTGTAGA        | 1153 – 1175        |
| SEQ ID NO:330 | GCAAATGTGTGTGTATCGTGGAAATATAAA | 1195 – 1224        |
| SEQ ID NO:331 | AAATTATTGAGCTAGAAGACAG         | 1253 – 1274        |
| SEQ ID NO:332 | GCACACCAGGTAGAAAGCCAA          | 1312 – 1332        |
| SEQ ID NO:333 | GGCTAGTTCAGATGTAAGCAGTGAAA     | 1377 – 1402        |
| SEQ ID NO:334 | GTAATATTCTACATAACAGTAA         | 1445 – 1466        |
| SEQ ID NO:335 | GCAACGCTATTATATAAATTC          | 1474 – 1494        |
| SEQ ID NO:336 | GCTTATGGAGTAAGTTTTATGGAA       | 1501 – 1524        |

Table 19. Sequences and loci of oligonucleotides for identifying HPV 59

| SEQ ID NO:    | 5'→ 3'               | Locus in HPV |
|---------------|----------------------|--------------|
|               |                      | 59           |
| SEQ ID NO:337 | TTCTACTACTTCTTC      | 6643 – 6657  |
| SEQ ID NO:338 | ACTACTTCTTCTATTCCTAA | 6647 – 6666  |
| SEQ ID NO:339 | ACTTCTTCTATTCCTAATGT | 6650 – 6669  |

| TCTTCTATTCCTAATGTATACAC        | 6653 – 6675  |
|--------------------------------|--|
| ATGTATACACACCTACCAGT           | 6666 – 6685  |
| TAAAATAACATTAACTACAGAGG        | 6745 – 6767  |
| TACCACTATTTTGGAGGAT            | 6793 – 6811  |
| TGTTACACCACCTCCTACTGCTAGTT     | 6823 – 6848  |
| ATACCGTTTTGTTCAATCTGCT         | 6859 – 6880  |
| GGACACCGCACCGCCAGTT            | 6898 – 6916  |
| TTATGACAAACTAAAG               | 6928 - 6943  |
| AGCCCAAAGGGATGCACGGGAAA        | 1093 – 1115  |
| GCAGTATAGAAAACAGTAGTGAGAAAGCGG | 1143 – 1172  |
| CCATTACAAGAAATATCAGTAAATG      | 1196 – 1220  |
| GGTTAATAACAGTGCCAGACAGCG       | 1245 – 1268  |
| GGTAACCGTGGAGAATACTGGAAATG     | 1306 – 1331  |
| CTGTAGCGACAGCAGTAACATGGATG     | 1372 – 1397  |
| CCCACTAATCAATTGTTACAGTTA       | 1421 – 1444  |
| GGGTTATCATTTCAAGATTTGG         | 1499 - 1520  |
|                                | ATGTATACACACCTACCAGT TAAAATAACATTAACTACAGAGG TACCACTATTTTGGAGGAT TGTTACACCACCTCCTACTGCTAGTT ATACCGTTTTGTTCAATCTGCT GGACACCGCACCG |

Table 20. Sequences and loci of oligonucleotides for identifying HPV 61

| SEQ ID NO:    | 5'→ 3'                        | Locus in HPV       |
|---------------|-------------------------------|--------------------|
|               |                               | 61                 |
| SEQ ID NO:356 | CTGCTACATCCCCCC               | 6803 – 6817        |
| SEQ ID NO:357 | ACATCCCCCCTGTATCTGA           | 6808 – 6827        |
| SEQ ID NO:358 | CATCCCCCCTGTATCTGAA           | 6809 - 6828        |
| SEQ ID NO:359 | CCCCTGTATCTGAATATAAAGC        | 6815 – 6836        |
| SEQ ID NO:360 | CTGAATATAAAGCCACAAGC          | 6824 – 6843        |
| SEQ ID NO:361 | TAAAATACATTTAACCCCTGAAA       | 6903 – 6925        |
| SEQ ID NO:362 | TAAGGCCTTGTTGGATGAC           | 6951 – 6969        |
| SEQ ID NO:363 | TGTGGTACCACCACCTCTACCAGTT     | 6981 – 7006        |
| SEQ ID NO:364 | ATATAGGTTTTTGCAGTCCAGA        | 7017 – 7038        |
| SEQ ID NO:365 | GGGTGCTGCCCCGCCGCCC           | 7056 <i>-</i> 7077 |
| SEQ ID NO:366 | CTATGCCAAGTTATCC              | 7089 – 7104        |
| SEQ ID NO:367 | TGCACAGGATGACGCTGCAACGG       | 1038 – 1060        |
| SEQ ID NO:368 | CCTTGGTGGACAGTGAATTAAGTCCC    | 1115 – 1140        |
| SEQ ID NO:369 | GGACAGGACAGGCTAGGAGAAGGCTGTTT | 1168 – 1197        |
| SEQ ID NO:370 | TGTTTGAGCAAGATAGTGGC          | 1193 – 1212        |
| SEQ ID NO:371 | GGATGCGCAACATGAGGGGGGGGGGG    | 1263 – 1288        |
| SEQ ID NO:372 | GGCCGAGGCCACAGGTAACCAGGAAA    | 1335 – 1360        |
| SEQ ID NO:373 | GGCAGACATATTAGAGGTGTTTAAGG    | 1380 – 1405        |
| SEQ ID NO:374 | CTGTACAAATTCAAGGACCTATTTGG    | 1429 – 1454        |
| SEQ ID NO:375 | CTAGCATTTGGGGAGCTGGTA         | 1456 – 1476        |

Table 21. Sequences and loci of oligonucleotides for identifying HPV 62

| SEQ ID NO:    | 5'→ 3'                     | Locus in HPV |
|---------------|----------------------------|--------------|
|               | ·                          | 62           |
| SEQ ID NO:376 | CCGCCTCCACTGCTG            | 92 – 106     |
| SEQ ID NO:377 | GCCTCCACTGCTGCAGCAGA       | 94 – 113     |
| SEQ ID NO:378 | CTGCTGCAGCAGAATACACG       | 101 – 120    |
| SEQ ID NO:379 | GCAGAATACACGGCTACCAA       | 109 – 128    |
| SEQ ID NO:380 | CAGAATACACGGCTACCAAC       | 110 – 129    |
| SEQ ID NO:381 | CAAAATACAGTTAACCCCCGAAA    | 189 – 211    |
| SEQ ID NO:382 | CAAGGACCTTTTGGATGAC        | 237 – 255    |
| SEQ ID NO:383 | GGTTTTACCTCCCCCTTCCACTAGTT | 267 – 292    |
| SEQ ID NO:384 | ATATCACTATTTCGAGTCTCGG     | 303 – 324    |
| SEQ ID NO:385 | GGGGCTGCCTACCCGTCCC        | 342 – 360    |
| SEQ ID NO:386 | GTATGCGCAAATGACA           | 372 – 387    |

Table 22. Sequences and loci of oligonucleotides for identifying HPV 66

| SEQ ID NO:    | 5'→ 3'                         | Locus in<br>HPV 66 |
|---------------|--------------------------------|--------------------|
| SEQ ID NO:387 | CAGCTAAAAGCACAT                | 6680 – 6694        |
| SEQ ID NO:388 | CAGCTAAAAGCACATTAACT           | 6680 – 6699        |
| SEQ ID NO:389 | CTAAAAGCACATTAACTAAA           | 6683 - 6702        |
| SEQ ID NO:390 | TTAACTAAATATGATGCCCG           | 6694 - 6713        |
| SEQ ID NO:391 | CTAAATATGATGCCCGTGAA           | 6698 – 6717        |
| SEQ ID NO:392 | TAAAATAACCTTAACTGCAGAAG        | 6777 – 6799        |
| SEQ ID NO:393 | TAATACTTTATTAGACGAT            | 6825 - 6843        |
| SEQ ID NO:394 | CTTATCCCCACCAGTTGCAACTAGCT     | 6855 - 6880        |
| SEQ ID NO:395 | ATATAGGTATATTAAAAGCACA         | 6891 - 6912        |
| SEQ ID NO:396 | GGAACAGCCCCCTGCAGAA            | 6930 - 6948        |
| SEQ ID NO:397 | CCTGGCTAAATATAAG               | 6960 – 6975        |
| SEQ ID NO:398 | AGCACATGCAGATGCACAGACG         | 1116 - 1137        |
| SEQ ID NO:399 | GGTAGTCCCTTAAGTGATATTAGTAA     | 1165 – 1190        |
| SEQ ID NO:400 | GCAAACTGTGTACCGAGAGGAAGTAA     | 1194 – 1219        |
| SEQ ID NO:401 | AAGGCTAATATTATCAGAAGACAGCGGGTA | 1224 – 1253        |
| SEQ ID NO:402 | GAAACATCACAACAGGTAGAATACG      | 1276 – 1300        |
| SEQ ID NO:403 | GAGCTCACAAAATGGAGGCTCGCAAA     | 1320 – 1345        |
| SEQ ID NO:404 | ATCAAATATGGATATAGATACAAATA     | 1371 – 1396        |
| SEQ ID NO:405 | CCAATTGCAGGAACTATTTAAAAGTA     | 1413 – 1438        |
| SEQ ID NO:406 | CAAGGAAGATTACATTTTAAATTTAA     | 1447 - 1472        |
| SEQ ID NO:407 | AGAAGTGTATGGAGTGCCAT           | 1473 – 1492        |

Table 23. Sequences and loci of oligonucleotides for identifying HPV 67

| SEQ ID NO: | 5'→ 3' | Locus in HPV |
|------------|--------|--------------|
|            |        | 67           |

| CTGAGGAAAAATCAG                | 6655 - 6669  |
|--------------------------------|--|
| GAGGAAAAATCAGAGGCTAC           | 6657 – 6676  |
| ATCAGAGGCTACATACAAAAATG        | 6665 – 6687  |
| AGGAAAAATCAGAGGCTACA           | 6658 - 6677  |
| CTACATACAAAAATGAAAAC           | 6673 – 6692  |
| CAAAATATCCCTTACTGCAAATG        | 6752 – 6774  |
| TCCAGATATATTAGAGGAC            | 6800 - 6818  |
| CCTTACACCACCTCCTTCAGGTAATT     | 6830 - 6855  |
| ATATAGATTTGTTACCTCGCAG         | 6866 – 6887  |
| AACATCCCCTCCAACAGCA            | 6905 - 6923  |
| TCTTAAAAAGTACAGT               | 6935 - 6950  |
| AGAGGAGGATGACCTAAACGCTG        | 1096 – 1118  |
| CAGGCATGTGGTGGTAATAGTAATGG     | 1151 – 1176  |
| GCCGCAAAACGCAGAGCATACGACATAGAA | 1199 – 1228  |
| GGCAAAATGGCGATATGCAGTGCAGT     | 1287 – 1312  |
| GCAAGTAGTACGGGAAACAGTGTAGA     | 1331 – 1356  |
| GTCAGGAACAAAGCATGCCATTGCAA     | 1380 – 1405  |
| GCATGTAAATAATATAAAGGCAACG      | 1423 – 1447  |
| GGAAGCATATGGGGTAACGTTTACAC     | 1465 – 1490  |
|                                | GAGGAAAAATCAGAGGCTAC ATCAGAGGCTACATACAAAAATG AGGAAAAATCAGAGGCTACA CTACATACAAAAATGAAAAC CAAAATATCCCTTACTGCAAATG TCCAGATATATTAGAGGAC CCTTACACCACCTCCTTCAGGTAATT ATATAGATTTGTTACCTCGCAG AACATCCCCTCCAACAGCA TCTTAAAAAGTACAGT AGAGGAGGATGACCTAAACGCTG CAGGCATGTGGTGGTAATAGTAATGG GCCGCAAAACGCAGGAATACGACATAGAA GGCAAAATGCCGATATGCAGTGCAG |

Table 24. Sequences and loci of oligonucleotides for identifying HPV 68

| SEQ ID NO:    | £2 . 22                        | T .         |
|---------------|--------------------------------|-------------|
| SEQ ID NO.    | 5'→ 3'                         | Locus in    |
|               |                                | HPV 68      |
| SEQ ID NO:427 | CTACTACTGAATCAG                | 2653 – 2667 |
| SEQ ID NO:428 | TGAATCAGCTGTACCAAATA           | 2660 - 2679 |
| SEQ ID NO:429 | GAATCAGCTGTACCAAATAT           | 2661 - 2680 |
| SEQ ID NO:430 | CAGCTGTACCAAATATTTATGA         | 2665 - 2686 |
| SEQ ID NO:431 | ATATTTATGATCCTAATAAA           | 2677 – 2696 |
| SEQ ID NO:432 | TCCTGCTATTTTGGATGAT            | 2804 - 2822 |
| SEQ ID NO:433 | TACTATAACATTGTCCACTGATG        | 2756 - 2778 |
| SEQ ID NO:434 | TGTTGCCCCTCCACCATCTGCTAGTC     | 2834 - 2859 |
| SEQ ID NO:435 | ATACCGCTATCTGCAATCAGCA         | 2870 - 2891 |
| SEQ ID NO:436 | AGACGCCCTGCACCTACT             | 2909 - 2927 |
| SEQ ID NO:437 | ATATGATGGCTTAAAC               | 2939 – 2954 |
| SEQ ID NO:438 | GGCCCAAAGGGATGCACAAACAG        | 4990 - 5012 |
| SEQ ID NO:439 | GCCCTTTAGCAAAGTCGCCATTACAG     | 5055 - 5080 |
| SEQ ID NO:440 | GGTAACTGTAGCAACTAATA           | 5115 - 5134 |
| SEQ ID NO:441 | GGAAAATGGCGACAGCATACGGGAGGACTG | 5163 - 5192 |
| SEQ ID NO:442 | GACAGTGCTATAGATAGTGAAAACCA     | 5203 - 5228 |
| SEQ ID NO:443 | CCTACTACGCAACTAAAAGTATTA       | 5242 - 5265 |
| SEQ ID NO:444 | AAGCTGCAATGTTAACAGAATTTAAA     | 5285 - 5310 |

Table 25. Sequences and loci of oligonucleotides for identifying HPV 69

| SEQ ID NO:    | 5'→ 3'                     | Locus in HPV |
|---------------|----------------------------|--------------|
|               |                            | 69           |
| SEQ ID NO:445 | TATTAGTACTGTATCTGCAC       | 6572 – 6591  |
| SEQ ID NO:446 | CTGTATCTGCACAAT            | 6580 – 6594  |
| SEQ ID NO:447 | CTGTATCTGCACAATCTGCA       | 6580 – 6599  |
| SEQ ID NO:448 | TGCACAATCTGCATCTGCCA       | 6587 – 6606  |
| SEQ ID NO:449 | CAATCTGCATCTGCCACTTTTA     | 6591 – 6612  |
| SEQ ID NO:450 | CCACTTTTAAACCATCAGAT       | 6604 – 6623  |
| SEQ ID NO:451 | TAAAATTACTCTTACCACTGATG    | 6683 – 6705  |
| SEQ ID NO:452 | TTCTACTATTTTGGAAAAT        | 6731 – 6749  |
| SEQ ID NO:453 | CCTTACCTTGCCTCCTACTGCTAGTT | 6761 – 6786  |
| SEQ ID NO:454 | ATATAGGTTTATTAAAAATTCA     | 6797 – 6818  |
| SEQ ID NO:455 | CGATGCCCTGCACAGCCC         | 6836 – 6854  |
| SEQ ID NO:456 | AACACAAGCAAATAAGAAGGCAG    | 1101 – 1123  |
| SEQ ID NO:457 | GAACAGCCCGTTGCAAGACATAACAA | 1158 – 1183  |
| SEQ ID NO:458 | CAGACGAAGTAAACAATTTACAGGC  | 1208 – 1232  |
| SEQ ID NO:459 | GGAGAGCAGTGGACAGCG         | 1238 – 1267  |
| SEQ ID NO:460 | GGTAGATAAACACAATGAACAAAATG | 1308 – 1333  |
| SEQ ID NO:461 | TCAAGTGGATCTGTATCAGACA     | 1360 – 1381  |
| SEQ ID NO:462 | GCACAGGCAAGTAGTGTAACCAAAA  | 1399 – 1423  |
| SEQ ID NO:463 | GTAATGTAAAAGCAGCATTATTAA   | 1445 – 1468  |
| SEQ ID NO:464 | CAGTATATGGTGTAAGTTATA      | 1481 – 1501  |

Table 26. Sequences and loci of oligonucleotides for identifying HPV 6

| SEQ ID NO:    | 5'→ 3'                         | Locus in    |
|---------------|--------------------------------|-------------|
|               |                                | HPV 6       |
| SEQ ID NO:465 | CATCCGTAACTACATCTTCC           | 6814 – 6833 |
| SEQ ID NO:466 | ATCCGTAACTACATCTTCCA           | 6815 – 6834 |
| SEQ ID NO:467 | CTACATCTTCCACATACACCAA         | 6823 – 6844 |
| SEQ ID NO:468 | CATCTTCCACATACACCAAT           | 6826 – 6845 |
| SEQ ID NO:469 | ATCTTCCACATACACCAATT           | 6827 – 6846 |
| SEQ ID NO:470 | CCACATACACCAATTCTGAT           | 6832 - 6851 |
| SEQ ID NO:471 | TAGCATTACATTGTCTGCTGAAG        | 6911 – 6933 |
| SEQ ID NO:472 | TCCCTCTGTTTTGGAAGAC            | 6959 – 6977 |
| SEQ ID NO:473 | GTTATCGCCTCCCCAAATGGTACAT      | 6989 – 7014 |
| SEQ ID NO:474 | CTATAGGTATGTGCAGTCACAG         | 7025 - 7046 |
| SEQ ID NO:475 | GCCCACTCCTGAAAAGGAA            | 7064 - 7082 |
| SEQ ID NO:476 | CTATAAGAACCTTAGT               | 7094 – 7109 |
| SEQ ID NO:477 | GGCGGACACCCATTATGCGACTG        | 1045 – 1067 |
| SEQ ID NO:478 | GTTAGTCCTATAAACACTATAGCCGA     | 1106 – 1131 |
| SEQ ID NO:479 | CCACGATTGGACGCCATTAAACTTACAAGA | 1154 – 1183 |
| SEQ ID NO:480 | GGCTGTTTCAAACCAGGGAACTAACG     | 1206 – 1231 |
| SEQ ID NO:481 | GGTAGAGAAACATGGCGTACCGGAAA     | 1279 – 1304 |

| SEQ ID NO:482 | GGACACAGGAAGGGACATAGAGGGGG | 1327 – 1352 |
|---------------|----------------------------|-------------|
| SEQ ID NO:483 | CACAAACAGTGTACGGGAGCATGCAG | 1378 – 1403 |
| SEQ ID NO:484 | GCTAAAATGTAAAGATTTACGGGCAG | 1426 – 1451 |
| SEQ ID NO:485 | GCTTTGGGCTGTCTTTTATAGATTTA | 1476 - 1501 |

Table 27. Sequences and loci of oligonucleotides for identifying HPV 70

| SEQ ID NO:    | 5'→ 3'                         | Locus in HPV |
|---------------|--------------------------------|--------------|
|               |                                | 70           |
| SEQ ID NO:486 | TGTCTGCCTGCACCGAAACG           | 6614 – 6633  |
| SEQ ID NO:487 | CTGCACCGAAACGGC                | 6621 – 6635  |
| SEQ ID NO:488 | GAAACGGCCATACCTGCTGT           | 6628 – 6647  |
| SEQ ID NO:489 | CGAAACGCCATACCTGCTG            | 6627 – 6646  |
| SEQ ID NO:490 | CGGCCATACCTGCTGTATATAG         | 6632 – 6653  |
| SEQ ID NO:491 | CTGTATATAGCCCTACAAAG           | 6644 – 6663  |
| SEQ ID NO:492 | TACTATCACATTAACTGCTGACG        | 6723 – 6745  |
| SEQ ID NO:493 | TCCTGCAATTTTGGACAAT            | 6771 – 6789  |
| SEQ ID NO:494 | AGTTACCCCTCCACCATCTGCAAGCT     | 6801 - 6826  |
| SEQ ID NO:495 | GTATAGGTATTTACAATCAGCA         | 6837 – 6858  |
| SEQ ID NO:496 | GGATGCTCCTACACCTGAA            | 6876 - 6894  |
| SEQ ID NO:497 | CTATGACGATTTAAAA               | 6906 – 6921  |
| SEQ ID NO:498 | GGCCCAAAGGGATGCACAATCAG        | 1149 – 1171  |
| SEQ ID NO:499 | GCAATCTAAATAAAAGTCCTTGT        | 1202 - 1224  |
| SEQ ID NO:500 | GTACATAGGGAACAAAGGGTAACAC      | 1240 – 1264  |
| SEQ ID NO:501 | GGTAAACATATGCAATAAACAGG        | 1278 - 1300  |
| SEQ ID NO:502 | ACAAACGTGTATTCAGTACCAGACAGCGGC | 1306 – 1335  |
| SEQ ID NO:503 | GTAGTAAATAATACAAATGGGGAAGA     | 1378 – 1403  |
| SEQ ID NO:504 | GGAGTGCAGTAGTGTAGACAGTGCTA     | 1446 – 1471  |
| SEQ ID NO:505 | TCCACAGTCACCTACTGCACAGCTAA     | 1491 – 1516  |
| SEQ ID NO:506 | GCTAATAACCAAAAAGCCATACTAC      | 1531 – 1555  |
| SEQ ID NO:507 | CACACATATGGATTAGCATTTAACGA     | 1570 – 1595  |

Table 28. Sequences and loci of oligonucleotides for identifying HPV 72

| SEQ ID NO:    | 5'→ 3'                  | Locus in HPV 72 |
|---------------|-------------------------|-----------------|
| SEQ ID NO:508 | ATCTGTTGGTTTAATGAGCT    | 6759 – 6778     |
| SEQ ID NO:509 | TTTGTGACAGTTGTAGATAC    | 6780 - 6799     |
| SEQ ID NO:510 | CTGCCACAGCGTCCT         | 6829 - 6843     |
| SEQ ID NO:511 | ACAGCGTCCTCTGTATCAGA    | 6834 – 6853     |
| SEQ ID NO:512 | CCACAGCGTCCTCTGTATCA    | 6832 - 6851     |
| SEQ ID NO:513 | AGCGTCCTCTGTATCAGAATAT  | 6836 – 6857     |
| SEQ ID NO:514 | CAGAATATACAGCTTCTAAT    | 6850 - 6869     |
| SEQ ID NO:515 | TAAAATTCACTTAACTCCTGAAA | 6929 – 6951     |

| SEQ ID NO:516 | TAAGGCCTTATTGGATGAC        | 6977 – 6995 |
|---------------|----------------------------|-------------|
| SEQ ID NO:517 | TGTGGTGCCTCCTCCTTCTACCAGTT | 7007 - 7032 |
| SEQ ID NO:518 | CTATAGGTTTTTGCAGTCTCGT     | 7043 - 7064 |
| SEQ ID NO:519 | GGGGCTGCCACCCCTCCTC        | 7082 - 7103 |
| SEQ ID NO:520 | ATATGCTAACTTATCC           | 7115 – 7130 |

Table 29. Sequences and loci of oligonucleotides for identifying HPV 74

| SEQ ID NO:    | 5'→ 3'                    | Locus in HPV |
|---------------|---------------------------|--------------|
|               |                           | 74           |
| SEQ ID NO:521 | CCTACCTCACAATCG           | 1686 - 1700  |
| SEQ ID NO:522 | CTCACAATCGCCTTCTGCTA      | 1691 – 1710  |
| SEQ ID NO:523 | ACCTCACAATCGCCTTCTGC      | 1689 – 1708  |
| SEQ ID NO:524 | CAATCGCCTTCTGCTACATATA    | 1695 – 1716  |
| SEQ ID NO:525 | ACAATCGCCTTCTGCTACATAT    | 1694 - 1715  |
| SEQ ID NO:526 | CTACATATAATAGTTCAGAC      | 1708 - 1727  |
| SEQ ID NO:527 | TAGTATTAAGTTAACTGCTGAGG   | 1787 – 1809  |
| SEQ ID NO:528 | TCCTACAGTTTTAGAAGAG       | 1835 –1853   |
| SEQ ID NO:529 | GCTAACGCCTCCCCCAATGGTACTT | 1865 - 1890  |
| SEQ ID NO:530 | CTACAGATATGTGCAGTCCCAG    | 1901 – 1922  |
| SEQ ID NO:531 | ACCTACGCCTGATAAAGCA       | 1940 – 1958  |
| SEQ ID NO:532 | CTATGCAAATTTAAGT          | 1970 – 1985  |

Table 30. Sequences and loci of oligonucleotides for identifying HPV 82

| SEQ ID NO:    | 5'→ 3'                         | Locus in HPV<br>82 |
|---------------|--------------------------------|--------------------|
| SEQ ID NO:533 | TGCTGTTACTCCATC                | 6608 - 6622        |
| SEQ ID NO:534 | TGCTGTTACTCCATCTGTTG           | 6608 – 6627        |
| SEQ ID NO:535 | ACTCCATCTGTTGCACAAAC           | 6615 – 6634        |
| SEQ ID NO:536 | AAACATTTACTCCAGCAAAC           | 6631 – 6650        |
| SEQ ID NO:537 | TAAAATCACTTTAACTACTGAAA        | 6710 – 6732        |
| SEQ ID NO:538 | TTCTACAATTTTAGAACAG            | 6758 – 6776        |
| SEQ ID NO:539 | ATTAACATTGCCCCCCTCCGCTAGTT     | 6788 – 6813        |
| SEQ ID NO:540 | CTATCGATTTGTAAAAAATGCA         | 6824 – 6845        |
| SEQ ID NO:541 | GGACAGTCCTCCACAGGCT            | 6863 – 6881        |
| SEQ ID NO:542 | AACACAGGCACACAAAGAGGCTG        | 1094 – 1116        |
| SEQ ID NO:543 | GCAGCCCATTAAAAGACATTACAAA      | 1156 – 1180        |
| SEQ ID NO:544 | GTCAGCAACAACCAAAACAGGCAAACCTTC | 1201 - 1230        |
| SEQ ID NO:545 | GGAGATTACTGGACAGTTATCCGGACA    | 1243 – 1269        |
| SEQ ID NO:546 | CCTTACAGGTAGATGGCCAAAATGAC     | 1309 – 1334        |
| SEQ ID NO:547 | GAGCAGCGACAGAAGTACAGAGATAG     | 1367 – 1392        |
| SEQ ID NO:548 | GCTACCAATGTAGGACTAAACAGTA      | 1413 – 1437        |
| SEQ ID NO:549 | GTAGCAATGCAAAAGCAATGTTTATG     | 1456 – 1481        |

| SEQ ID NO:550 | GGTGTTAGTTATAATGAGTTGGTAAG | 1502 1520   |
|---------------|----------------------------|-------------|
| BLQ ID NO.330 | OGIGITAGITATAATOAGITGGTAAG | 1303 - 1326 |

Table 31. Sequences and loci of oligonucleotides for identifying HPV CP8061

| SEQ ID NO:    | 5'→ 3'                  | Locus in HPV<br>CP8061 |
|---------------|-------------------------|------------------------|
| SEQ ID NO:551 | TCTGTGCTACCAAAACTGTT    | 86 – 105               |
| SEQ ID NO:552 | CTACCAAAACTGTTG         | 92 – 106               |
| SEQ ID NO:553 | ACCAAAACTGTTGAGTCTAC    | 94 – 113               |
| SEQ ID NO:554 | AACTGTTGAGTCTACATATAAA  | 99 – 120               |
| SEQ ID NO:555 | GTTGAGTCTACATATAAAGC    | 103 – 122              |
| SEQ ID NO:556 | CTACATATAAAGCCTCTAGT    | 110 – 129              |
| SEQ ID NO:557 | TGTTATTAATTTAACAGCTGAAA | 189 – 211              |
| SEQ ID NO:558 | TGCTACATTACTGGAGGAC     | 237 – 255              |
| SEQ ID NO:559 | GTTCTTACCACCTCCTACTG    | 267 – 286              |
| SEQ ID NO:560 | CTACCGCTTTTTACAGTCTCAG  | 303 – 324              |
| SEQ ID NO:561 | AAACAGTCCTCCTCCTGCAGAA  | 342 – 363              |
| SEQ ID NO:562 | CTATGCAGATCTTACA        | 375 – 390              |

# 5 Table 32. Sequences and loci of oligonucleotides for identifying

## **HPV CP8034**

| C1 005 1      |                            |              |
|---------------|----------------------------|--------------|
| SEQ ID NO:    | 5'→ 3'                     | Locus in HPV |
|               |                            | CP8034       |
| SEQ ID NO:563 | CAGCTACATCTGCTG            | 92 - 106     |
| SEQ ID NO:564 | GCTACATCTGCTGCTGCAGA       | 94 – 113     |
| SEQ ID NO:565 | ACATCTGCTGCTGCAGAATACA     | 97 - 118     |
| SEQ ID NO:566 | TGCTGCAGAATACAAGGCCT       | 105 – 124    |
| SEQ ID NO:567 | GCTGCAGAATACAAGGCCTC       | 106 – 125    |
| SEQ ID NO:568 | CAGAATACAAGGCCTCTAAC       | 110 – 129    |
| SEQ ID NO:569 | TAAAATACAGTTAACACCAGAAA    | 189 - 211    |
| SEQ ID NO:570 | CAAGGCACTGTTGGATGAT        | 237 – 255    |
| SEQ ID NO:571 | TGTGTTGCCACCTCCTTCCACCAGTT | 267 – 292    |
| SEQ ID NO:572 | ATATCGCTTTTTACAGTCTCGG     | 303 – 324    |
| SEQ ID NO:573 | GGGTGCTGCCCCTGCGCCC        | 342 – 363    |
| SEQ ID NO:574 | TTATGCCGACATGTCA           | 375 – 390    |
|               |                            |              |

Table 33. Sequences and loci of oligonucleotides for identifying

## 10 HPV L1AE5

| SEQ ID NO:    | 5'→ 3'               | Locus in HPV |
|---------------|----------------------|--------------|
|               |                      | L1AE5        |
| SEQ ID NO:575 | ATCTACTGCAACTACTAATC | 69 ~ 88      |

| SEQ ID NO:576 | CTGCAACTACTAATC           | 74 – 88   |
|---------------|---------------------------|-----------|
| SEQ ID NO:577 | CTGCAACTACTAATCCAGTT      | 74 – 93   |
| SEQ ID NO:578 | ACTACTAATCCAGTTCCATCTA    | 79 – 100  |
| SEQ ID NO:579 | CTAATCCAGTTCCATCTATA      | 83 – 102  |
| SEQ ID NO:580 | CTATATATGAACCTTCTAAA      | 98 – 117  |
| SEQ ID NO:581 | TAAAATTACACTTACTACTGATG   | 177 – 199 |
| SEQ ID NO:582 | TCCTACTATTTTAGATAGT       | 225 – 243 |
| SEQ ID NO:583 | TGTTAGTCCTCCCCATCTGCTAGCT | 255 – 280 |
| SEQ ID NO:584 | ATATAGGTTTTTACAGTCATCT    | 291 – 312 |
| SEQ ID NO:585 | GGATGTGGTTGTTCCACAA       | 330 – 348 |

Table 34. Sequences and loci of oligonucleotides for identifying

# HPV MM4

| SEQ ID NO:    | 5'→ 3'                     | Locus in HPV |
|---------------|----------------------------|--------------|
|               |                            | MM4          |
| SEQ ID NO:586 | CTGCTGTTACTCAATCTGTT       | 92 – 111     |
| SEQ ID NO:587 | TGCTGTTACTCAATC            | 93 – 107     |
| SEQ ID NO:588 | GTTACTCAATCTGTTGCACA       | 97 – 116     |
| SEQ ID NO:589 | TGCACAAACATTTACTCCAG       | 111 – 130    |
| SEQ ID NO:590 | TTACTCAATCTGTTGCACAAAC     | 98 – 119     |
| SEQ ID NO:591 | AAACATTTACTCCAGCAAAC       | 116 – 135    |
| SEQ ID NO:592 | TAAAATCACTTTAACTACTGAAA    | 195 – 217    |
| SEQ ID NO:593 | TTCTACAATTTTAGAACAG        | 243 – 261    |
| SEQ ID NO:594 | ATTAACCTTGCCCCCCTCAGCTAGTT | 273 – 298    |
| SEQ ID NO:595 | CTATCGATTTGTAAAAAATGCA     | 309 – 330    |
| SEQ ID NO:596 | GGACAGTCCTCCACAGGCT        | 348 – 366    |

# 5 Table 35. Sequences and loci of oligonucleotides for identifying

# HPV MM7

| SEQ ID NO:    | 5'→ 3'                     | Locus in HPV<br>MM7 |
|---------------|----------------------------|---------------------|
| SEQ ID NO:597 | TGCTGCTACACAGGC            | 93 – 107            |
| SEQ ID NO:598 | GCTGCTACACAGGCTAATGA       | 94 – 113            |
| SEQ ID NO:599 | TGCTACACAGGCTAATGAAT       | 96 – 115            |
| SEQ ID NO:600 | CTACACAGGCTAATGAATACAC     | 98 – 119            |
| SEQ ID NO:601 | ATGAATACACAGCCTCTAAC       | 110 – 129           |
| SEQ ID NO:602 | CAAAATACATCTTACCCCTGAAA    | 189 – 211           |
| SEQ ID NO:603 | TGAACATTTATTGGATGAG        | 237 – 255           |
| SEQ ID NO:604 | CGTGTTACCACCTCCTTCCACCAGCC | 267 – 292           |
| SEQ ID NO:605 | CTATCGCTATCTGCAGTCCCGT     | 303 - 324           |
| SEQ ID NO:606 | GGGTCCTTCCGCCCCTGCCCCT     | 342 – 363           |
| SEQ ID NO:607 | TTATGATGGCCTTGTA           | 375 – 390           |

Table 36. Sequences and loci of oligonucleotides for identifying

# HPV MM8

| SEQ ID NO:    | 5'→ 3'                     | Locus in HPV |
|---------------|----------------------------|--------------|
|               |                            | M[M8         |
| SEQ ID NO:608 | TGCTACCAACACCGA            | 93 –107      |
| SEQ ID NO:609 | CTACCAACACCGAATCAGAA       | 95 –114      |
| SEQ ID NO:610 | CCAACACCGAATCAGAATATAA     | 98 –119      |
| SEQ ID NO:611 | CAGAATATAAACCTACCAAT       | 110 – 129    |
| SEQ ID NO:612 | TAAGGTCCGTCTGACTCCAGAGG    | 189 – 211    |
| SEQ ID NO:613 | TGACTCCTTATTAGATGAG        | 237 - 255    |
| SEQ ID NO:614 | TGTTGTGCCCCCTCCCTCCACAAGTT | 267 – 292    |
| SEQ ID NO:615 | CTATAGGTACTTGCAGTCTCGC     | 303 – 324    |
| SEQ ID NO:616 | GGGGCCGCCGCCAAGCCT         | 342 – 363    |
| SEQ ID NO:617 | TTATGCTGGCATGTCC           | 375 – 390    |

# 5 Table 37. Sequences and loci of oligonucleotides for identifying

# HPV 42

| SEQ ID NO:    | 5'→ 3'                         | Locus in<br>HPV 42 |
|---------------|--------------------------------|--------------------|
| SEQ ID NO:618 | TATATGTTGGGGAAATCAGCTA         | 6802 - 6823        |
| SEQ ID NO:619 | CACTGCAACATCTGGTGATA           | 6874 - 6893        |
| SEQ ID NO:620 | GCAACATCTGGTGATACATATACAGCTGCT | 6878 - 6907        |
| SEQ ID NO:621 | CATTAACTGTTGAAGTTATGTCA        | 6978 - 7000        |
| SEQ ID NO:622 | CCTAACATATTAGAGGAGTGGAATGT     | 7019 - 7044        |
| SEQ ID NO:623 | CACCACCACCTTCAGGAACT           | 7053 - 7072        |
| SEQ ID NO:624 | GTTATAGGTATGTACAATCAGAAG       | 7083 - 7106        |
| SEQ ID NO:625 | GCTAAGGTAACAACGCCAGAAAAAAAGGAT | 7121 - 7150        |
| SEQ ID NO:626 | CAGACTTTTGGTTTTGGGAGGTAA       | 7158 - 7181        |
| SEQ ID NO:627 | GAAAAGTTTTCTACTGATTTA          | 7190 - 7210        |
| SEQ ID NO:628 | GTCAGTGATTCACAGCACAGCATAG      | 1111 - 1135        |
| SEQ ID NO:629 | GTCCTAGGCTTGGCGGTTTAA          | 1148 - 1168        |
| SEQ ID NO:630 | CCCAAGGGCCAAACGACGATTATTCCAGT  | 1184 - 1213        |
| SEQ ID NO:631 | CAGCAGACACAGGTAGAACACGGACA     | 1261 - 1286        |
| SEQ ID NO:632 | GCAGTGGGTAGTGAACTTGGGG         | 1321 - 1342        |
| SEQ ID NO:633 | GAAGAAGGTAGTACTACAAGTACGCC     | 1354 - 1379        |
| SEQ ID NO:634 | GGTAGAATTACTTAAGTGTAAGAAC      | 1392 - 1416        |
| SEQ ID NO:635 | GTTAGGTAAGTTTAAAGAATTG         | 1431 - 1452        |
| SEQ ID NO:636 | GTCATTTGGCGATTTAGTAAGA         | 1461 - 1482        |

Table 38. Sequences and loci of oligonucleotides for identifying HPV 43

| SEQ ID NO:    | 5'→ 3'                         | Locus in<br>HPV 43 |
|---------------|--------------------------------|--------------------|
| SEQ ID NO:637 | CATTTGTTTTGGGAATCAGTTG         | 21 - 42            |
| SEQ ID NO:638 | TGACCCTACTGTGCCCAGTA           | 99 - 118           |
| SEQ ID NO:639 | ACTGTGCCCAGTACATATGACAATGCAAAG | 106 - 135          |
| SEQ ID NO:640 | GTTTATATTTCAATTATGCATAA        | 177 - 199          |
| SEQ ID NO:641 | CCAGAGGTTATGACATATATT          | 211 – 231          |
| SEQ ID NO:642 | CCCACATTATTAGAGGACTGGAA        | 244 - 266          |
| SEQ ID NO:643 | CCACCTGCCTCTGCTTCTTTG          | 280 - 300          |
| SEQ ID NO:644 | CGCTTTTTGTCTAACAAGGCCATTG      | 313 – 337          |
| SEQ ID NO:645 | CCAAAGGAACGGGAGGATCCCTA        | 358 - 380          |
| SEQ ID NO:646 | CTTACAGAAAAGTTTTCTGCACAAC      | 409 - 433          |

Each dot on the carrier 11 is an oligonucleotide selected from Tables 1 to 36. For example, an oligonucleotide on the carrier 11 could be selected from one of the sequences numbered SEQ ID NO: 1 to SEQ ID NO 24(shown in Table 1) for indentifying the subtype 11 of human papilloma viruses (HPV 11).

The method for mounting the oligonucleotides on the carrier 11 (the nylon membrane) is described as follows.

1.-TTTTTTTTTTTTT (SEQ ID NO: 647) is added to the 3' end of the oligonucleotide provided by the present invention by terminal transferase according to the following steps 1.1 to 1.3.

| 1.1 Mixing the following components: 10X NEBuffer 4              | 5 μl                      |
|--|---------------------------|
| 2.5 mM CoCl <sub>2</sub>   | 5 μl                      |
| oligonucleotide  | $5 \sim 300 \text{ pmol}$ |
| $10 \sim 300 \ mM \ dATP$ $ \cdot  dCTP  \cdot  dTTP \ or  dGTP$ | 1 μl                      |
| Terminal Transferase (20U/ul) (NEW English                       | $0.5 \sim 5 \mu l$        |
| BioLabs,M0252S)  |                           |
| Add M.Q. H <sub>2</sub> O to final volume                        | 50 μl                     |

1.2 The components are mixed at 37°C for 15~60 minutes.

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 $1.3\,10\,\mu l$  of  $0.2\,M$  EDTA (pH 8.0) is added to the mixture to stop the reaction.

- 2. The oligonucleotide having 3' end labeling is mounted on the carrier 11 according to the following steps 2.1 to 2.3.
- 2.1 The oligonucleotide having 3' end labeling is mounted on the carrier 11 by a needle having a 400  $\mu$ m wide head. The distance between each dot is 1200  $\mu$ m.
- 5 2.2 The carrier 11 having the dot array 12 thereon is exposed to UV light, and the detector 10 is formed.
  - 2.3 The detector 10 is preserved in a drying box.

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Please refer to Fig. 2. A detector 20 is the second embodiment of the present invention for simultaneously detecting and identifying subtypes of human papilloma viruses contained in a sample. The detector 20 includes a carrier 21 and a dot array 22. The carrier 21 is a glass plate having the dot array 22 mounted thereon. Each dot in the dot array 12 is an oligonucleotide (15~30mer) for identifying a specific subtype of human papilloma viruses.

Each dot on the carrier 21 is an oligonucleotide selected from Tables 1 to 36. For example, an oligonucleotide on the carrier 21 could be selected from one of the sequences numbered SEQ ID NO: 1 TO SEQ ID NO: 24 (shown in Table 1) for indentifying the subtype 11 of human papilloma viruses (HPV 11).

The method for mounting the oligonucleotides on the carrier 21 (the glass plate) is described as follows.

- 1. The surface of the carrier 21 is treated according to the following steps 1.1 to 1.8.
- 1.1 The carrier 21 is cleaned in non-fluorescent and soft cleaner.
- 1.2 The clean carrier 21 is immersed in 10% NaOH.
- 1.3 The carrier 21 is oscillated in double-distilled water, 1% HCl solution and methanol in sequence for 2 minutes, and dried in an oven.
- 1.4 The carrier 21 is immersed in 1% 3-aminopropyltrimethoxysilane (APTMS) in 95% aqueous acetone at room temperature for about 2 minutes.
  - 1.5 The carrier 21 is washed in acetone, and the carrier 21 is dried in the oven at 110°C for 45 minutes.

- 1.6 The dried carrier 21 is immersed in 0.2% 1,4-phenylene diisothiocyanate, wherein the solvent is 10% pyridine in dimethyl formamide), at room temperature for 2 hours.
  - 1.7 The carrier 21 is washed in methanol and acetone, and then the carrier 21 is dried.
  - 1.8 The dried carrier 21 is preserved in a vacuum and dry box.
- 2. The oligonucleotides provided by the present invention are mounted on the carrier 21 (the glass plate) according to the following steps 2.1 to 2.3.
- 2.1 The oligonucleotide having 3' end labeling is mounted on the carrier 21 by a needle having a 400  $\mu$ m wide head. The distance between each dot is 1200  $\mu$ m.
- 2.2 The carrier 21 is immersed in 1% NH<sub>4</sub>OH solution for about 2 minutes, washed in double-distilled water, and then dried at room temperature. Thus, the detector 20 is formed.
  - 2.3 The detector 20 is preserved in a dried box.

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The method provided by the present invention for simultaneously detecting and identifying subtypes of human papilloma viruses contained in a sample is described as follows.

- 1. The sample is treated according to the following steps 1.1 to 1.3.
- 1.1 The cells are centrifuged at 1,500 rpm at 20°C for 5 minutes.
- 1.2 The cell pellet is washed in 10 mM Tris (pH 8.5) and dissolved in 8 mM NaOH. Then, the solution is transfer to 1.5 mL micro-tube.
- 1.3 A proper amount of TreTaq ( $1U/\mu l$ ) solution is added to the micro-tube. The reaction is carried out at 95 °C for 1 hour. The DNA contained in the sample is obtained after centrifugation at 13,500 rpm, 20 °C for 5 minutes. The otained DNA is preserved at -20 °C.
- 2 Polymerase chain reactions are performed according to the following steps.
- 2.1 Glutaldehyde-3-phosphodehydrogenase gene is used as the internal control of the polymerase chain reactions according to the following steps 2.1.1 to 2.1.3.
- 2.1.1 Mixing the following components:

| Reagent                  | Stock  | amount | Final concentration |
|--------------------------|--|--------|---------------------|
| Sterile H <sub>2</sub> O | na nga pagasan ang ang ang ang ang ang ang ang ang a | 2.6    |                     |
| 10X Taq Buffer           |  | 0.5    | 1X Taq Buffer       |

| dNTP                          | 2.5 mM     | 0.4 | 200 μΜ                         |
|-------------------------------|------------|-----|--------------------------------|
| Template                      |            | 1   |                                |
| GAP241-5 <sup>1)</sup> primer | 10 pmol/μl | 0.2 | $0.4 \text{ pmol/}\mu\text{l}$ |
| GAP241-3 <sup>2)</sup> primer | 10 pmol/μl | 0.2 | $0.4 \text{ pmol/}\mu\text{l}$ |
| ProTaq                        | 5 U/μl     | 0.1 | 0.1 U/μΙ                       |
| (PROTECH)                     |            |     |                                |
| Total volume (µl)             |            | 5   |                                |

<sup>1)</sup> Gap21-5 (SEQ ID NO: 648): CCACCAACTGCTTAGCACCCC

<sup>2.1.2</sup> The polymerase chain reaction is performed according to the following programs.

| Program 1                   | Program 2         | Program 3 |  |
|-----------------------------|-------------------|-----------|--|
|                             | 94°C → 15 seconds |           |  |
| 94℃,                        | 57℃ ,             | 72℃,      |  |
| 3 minutes                   | 1 minute          | 5 minutes |  |
| $72^{\circ}$ C , 30 seconds |                   |           |  |
|                             | 40 cycles         |           |  |

<sup>2.1.3</sup> The product of the polymerase chain reaction is analyzed in 2.5% agarose/EtBr (0.5×TBE).

## 2.2.1 Mixing the following components:

| Reagent                  | Stock  | Amount  | Final         |
|--------------------------|--------|---------|---------------|
|                          |        |         | concentration |
| Sterile H <sub>2</sub> O |        | 4.7-5.7 | - 8           |
| 10X Taq Buffer           |        | 1       | 1X Taq Buffer |
| dNTP                     | 2.5 mM | 0.8     | 200 μΜ        |
| Template                 |        | 1-2     |               |

<sup>2)</sup> Gap21-3 (SEQ ID NO: 649): TGCAGCGTACTCCCCACATCA

<sup>3)</sup> The proper amount of mineral oil is added to prevent the evaporation.

<sup>2.2</sup> The DNA contained in the sample is proceeded the first round of polymerase chain reaction according to the following steps.

| BSA                           | 10 mg/ml   | 0.1 | 0.1 μg/μl   |
|-------------------------------|------------|-----|-------------|
| Primer <sup>1,2)</sup>        | 10 pmol/μl | 0.6 | 0.6 pmol/μl |
| Primer <sup>1,2)</sup>        | 10 pmol/μl | 0.6 | 0.6 pmol/μl |
| ProTaq (PRO <sub>TECH</sub> ) | 5 U/μl     | 0.2 | 0.1 U/μl    |
| Total volume                  |            | 10  |             |
| ( µl )                        |            | •   |             |

<sup>1)</sup> MY09/MY11: Manos et al., Cancer Cells 1989, 7, 209-214;

<sup>2.2.2</sup> The polymerase chain reaction is performed according to the following programs.

| Program 1                               | Program 2        | Program 3 |
|---|------------------|-----------|
|   | 94℃ , 45 seconds |           |
| 94°C,                                   | 45℃,             | 72℃,      |
| 3 minutes                               | 1 minute         | 5 minutes |
|   | 72℃,             |           |
|   | 1.5 minutes      |           |
| *************************************** | 45 cycles        |           |

<sup>2.2.3</sup> The product of the polymerase chain reaction is analyzed in 2.5% agarose/EtBr (0.5×TBE).

## 2.3.1 Mixing the following components:

| Reagent                  | Stock  | Amount | Final         |
|--------------------------|--------|--------|---------------|
|                          |        |        | concentration |
| Sterile H <sub>2</sub> O |        | 11.75  |               |
| 10X Taq Buffer           |        | 2.5    | 1X Taq Buffer |
| dNTP                     | 2.5 mM | 2      | 200 μΜ        |
| First round PCR          |        | 5      |               |
| product                  |        |        |               |

<sup>2)</sup> E1 301L/E1 847R: Ylitalo et al., J. Clin. Microbiol. 1995, 33, 1822-1828;

<sup>3)</sup> The proper amount of mineral oil is added to prevent the evaporation.

<sup>2.3</sup> The DNA contained in the sample is proceeded the second round of polymerase chain reaction via internal primers according to the following steps.

| BSA                           | 10 mg/ml   | 0.25 | $0.1 \mu g/\mu l$ |
|-------------------------------|------------|------|-------------------|
| Primer <sup>1)</sup>          | 10 pmol/μl | 1.5  | 0.6 pmol/μl       |
| Primer <sup>1,2,3)</sup>      | 10 pmol/μl | 1.5  | 0.6 pmol/µl       |
| ProTaq (PRO <sub>TECH</sub> ) | 5 U/μl     | 0.5  | 0.1 U/μl          |
| Final volumn (µl)             |            | 25   |                   |

- 1) GP5+/GP6+: De Roda Husman et al., J. Gen. Virol. 1995, 76, 1057-1062;
- 2) E1 350L/E1 547R: Ylitalo et al. J. Clin. Microbiol. 1995, 33, 1822-1828;
- 3) The 5' end of the GP6+ and E1 547R primers could be labeled with biotin or Cy5 fluorescent substances.
  - 4)The proper amount of mineral oil is added to present the evaporation.
  - 2.3.2 The polymerase chain reaction is performed according to the following programs.

| Program 1 | Program 2   | Program 3 |
|-----------|-------------|-----------|
|           | 94°C →      |           |
|           | 45 seconds  |           |
| 94°C ,    | 45°C ,      | 72°C ,    |
| 3 minutes | 1 minute    | 5 minutes |
|           | 72°C ,      |           |
|           | 1.5 minutes |           |
|           | 45 cycles   |           |

- 2.3.3 The product of the polymerase chain reaction is analyzed in 2.5% agarose/EtBr (0.5×TBE).
- 3. The detector 10 provided by the present invention is used for identifying the subtypes of human papilloma viruses according to the following steps.
  - 3.1 The detector 10 is immersed in 2x SSC solution for 5 minutes.
  - 3.2 The detector 10 is immersed in a buffer containing salmon sperm DNA (50  $\mu$ g/ $\mu$ l), and the oligonucleotides mounted on the detector 10 are pre-hybridized with the salmon sperm DNA at 35°C for 30 minutes.
- 3.3 The PCR product having biotin labeled thereon is added into and mixed with a buffer containing salmon sperm DNA (50 μg/μl) at 95°C for about 5 minutes. The denatured DNA is

placed on ice.

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- 3.4 The denature DNA is added to the detector 10 and hybridized with the oligonucleotides at 35°C for 4 hours or overnight.
  - 3.5 The detector 10 is washed in 2x SSC/1% SDS solution at 35°C for 15 minutes.
  - 3.6 The detector 10 is washed in 0.2x SSC/0.1% SDS solution at 35°C for 15 minutes.
  - 3.7 The detector 10 is treated in 0.5% isolation reagent for 1 hour.
  - 3.8 The detector 10 is treated with avidin-alkalinephosphatase for about 1 hour.
  - 3.9 The detector 10 is washed in 1x PBST solution.
  - 3.10 The detector 10 is washed in Tris/NaCl solution.
- 3.11 The detector 10 is treated with NBT/BCIP at room temperature to show the reacting dot in blue.
  - 3.12 The blue dot having the specific oligonucleotide sequence presents the specific subtype of human papilloma viruses contained in the sample.
  - 4. The detector 20 provided by the present invention is used for identifying the subtypes of human papilloma viruses according to the following steps.
  - 4.1 The PCR product having Cy5 labeled thereon is purified by PCR Clean Up-M System (Viogene, USA), and the PCR product is precipitated in ethanol. Then, the PCR product is dried.
  - 4.2 The precipitated DNA is dissolved in 12  $\mu$ l of the buffer (2x SSC/0.1% SDS), and centrifugated for 1 minute, and then placed on boiled water for 2 minutes. Then, the mixture is placed on ice for 5 minutes.
  - 4.3 The mixture is centrifugated for 30 seconds, and 10  $\mu$ l of the mixture is added to the left side of the dot array 22. A cover slice is carefully covered on the dot array from the left side of the dot array to prevent the bubble formation. Then, the detector 20 is place in Humid Chamber (Sigma, USA), and the dot array is faces downward at 35°C for 4 hours or overnight.
  - 4.4 The detector 20 is vertically placed in the solution A (2x SSC/1% SDS), and the detector is slightly oscillated apart from the cover slice. Then, the detector 20 is washed in a shaker at 160 rpm for 12 minutes.
- 4.5 The detector 20 is washed in the solution B (0.2x SSC/0.1% SDS) and oscillated at 35°C for 12 minutes. The detector 20 is washed in water. Then the detector 20 is dried.

4.6 The dried detector 20 is scanned by GenePix<sup>TM</sup>4000 (Axon, USA), excited by the light having 635 nm of wavelength, and analyzed by GenePixPro 3.0 (Axon, USA).

Please refer to Figs. 3(a) and (b). Fig. 3(a) is a schematic view showing the third embodiment of the present invention. The detector 30 provided by the present invention is used for simultaneously detecting and identifying subtypes of human papilloma viruses contained in a sample. The detector 30 includes a carrier 31 and a dot array 32.

The carrier 31 is a nylon membrane. The actual length of the nylon membrane is about 1.44 cm and the actual width of the nylon membrane is about 0.96 cm. The dot array is mounted on the carrier 31 according to the foresaid method, wherein the distance between each dot is about 1.2 mm and the diameter of each dot is about 0.4 mm. Each dot is an oligonucleotide (15~30mer), and each oligonucleotide is used for specifically identifying a subtype of human papilloma viruses. The sequence of the oligonucleotide is selected from the Tables 1 to 36.

The subtype of human papilloma viruses identified by each dot of the dot array 32 is illustrated in Fig. 3(b). SC (system control) presents the PCR product amplified from any subtype of human papilloma viruses and biotin-contained primer. NC (negative control) presents the plants DNA fragment irrelevant to HPV. IN (internal control) presents the sequence 5'-gcccagactgtgggtggcag-3' (SEQ ID NO: 650) of the housekeeping gene, Glyceraldehyde-3-Phosphate Dehydrogenase (GAP-DH).

The plural detector 30 are used for identifying positive clones of human papilloma viruses according to the foresaid method, and the results are shown in Figs. 4(a) to (c). The positive clones are respective amplified by using MY11/MY09 primers and the first round of polymerase chain reaction. The products of the first polymerase chain reaction are analyzed in 2.5% agarose/EtBr, and the electrophoresis results are shown in Fig. 4(a). The products of the first round polymerase chain reaction are respective amplified by using GP5/GP6 primers and the second round of polymerase chain reaction. The products of the second polymerase chain reaction are analyzed in 2.5% agarose/EtBr, and the electrophoresis results are shown in Fig. 4(b). The numbers labeled in Figs. 4(a) and (b) and the corresponding HPV clones are illustrated in Table 39.

Table 39

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| NO: | HPV clone  | NO: | HPV clone | NO: | HPV clone  |
|-----|------------|-----|-----------|-----|------------|
| М   | DNA marker | 7   | HPV 33    | 14  | HPV 56     |
| 1   | HPV 6      | 8   | HPV 35    | 15  | HPV 59     |
| 2   | HPV 11     | 9   | HPV 44    | 16  | HPV 61     |
| 3   | HPV 16     | 10  | HPV 45    | 17  | HPV 66     |
| 4   | HPV 18     | 11  | HPV 52    | 18  | HPV 70     |
| 5   | HPV 26     | 12  | HPV 53    | 19  | HPV CP8061 |
| 6   | HPV 31     | 13  | HPV 54    | 20  | HPV L1AE5  |

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The foresaid products numbered 1 to 20 of the second polymerase chain reactions are respectively detected by the detectors 30, and the results are shown in Fig. 4(c). According to the comparison between the results shown in Fig. 4 (c) and Fig. 3(b) based on the "SC" dot, the detector 30 provided by the present invention is used for precisely identifying the subtype of human papilloma viruses. Furthermore, no cross reactions occur in the detection.

In addition, the detectors 30 are used for detecting and identifying the subtypes of human papilloma viruses contained in a sample, and the results are shown in Fig. 5. According to the comparison between the results shown in Fig. 5 and Fig. 3(b) based on the "SC" dot, HPV 53 is contained in the sample (1), HPV 45 is contained in the sample (2), HPV 52 is contained in the sample (3), and HPV 39 is contained in the sample (4).

Please refer to Figs. 6(a) and (b). Fig. 6(a) is a schematic view showing the fourth embodiment of the present invention. The detector 40 is used for simultaneously detecting and identifying the subtypes of human papilloma viruses contained in a sample. The detector 40 includes a carrier 41 and a dot array 42. The carrier 41 is a glass plate, and the dot array 42 is mounted on the glass plate according to the foresaid method. Each dot is an oligonucleotide (15~30mer) for specifically identifying a subtype of human papilloma viruses. The sequences of the oligonucleotides are selected from Tables. 1 to 36. The subtype of human papilloma viruses identified by each dot of the dot array 42 is illustrated in Fig. 6(b).

The detector 40 is stained with SYBR Green II, scanned by GenePix<sup>TM</sup> 4000 (Axon, USA) and excited by the light having 635 nm of wavelength. The result is shown in Fig. 7(a).

In addition, the positive clones of HPV 11 and HPV 18 are respectively treated with two rounds of polymerase chain reactions, and the products of the polymerase chain reactions are

respectively analyzed by the detectors 40. The results are shown in Fig. 7(b), wherein the red fluorescent dot presents positive result. According to the comparison between the results shown in Fig. 7(b) and Fig. 6(b), the detector 40 provided by the present invention is used for precisely identifying the subtype of human papilloma viruses. Furthermore, no cross reactions occur in the detection.

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While the invention has been described in terms of what are presently considered to be the most practical and preferred embodiments, it is to be understood that the invention need not be limited to the disclosed embodiment. On the contrary, it is intended to cover various modifications and similar arrangements included within the spirit and scope of the appended claims which are to be accorded with the broadest interpretation so as to encompass all such modifications and similar structures. Therefore, the above description and illustration should not be taken as limiting the scope of the present invention which is defined by the appended claims.